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PULMONARY ATELECTASIS FOLLOWING THYROIDECTOMY

REPORT OF FOUR CASES WITH OBSERVATIONS AT NECROPSY *

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The opportunity to examine the lungs in four fatal cases of pulmonary atelectasis following operations on the thyroid gland has stimulated me to report my observations and to review the literature pertaining to this condition.

REPORT OF CASES

CASE 1.—A woman, aged 30, was admitted to the hospital with a condition which was diagnosed as hyperthyroidism and diabetes mellitus. Her basal metabolic rate was plus 75 per cent. Ten days after admission, a thyroidectomy was performed. The gland showed a slight hyperplasia. During the operation a stridor developed, but the condition improved, and the patient had a good voice when the operation was finished. On the following day, she suddenly became moderately cyanotic, and the respiratory rate became rapid; the temperature was 103.6 F.; the pulse rate was 146. An examination of the chest showed a good respiratory excursion on each side and normal breath sounds, except for moisture, on both sides. The apex beat of the heart was in the anterior axillary line on the left side. The vocal cord on the left side was paralyzed. A tracheotomy was performed without any effect on the cyanosis. The pulse rate and the difficulty in respiration gradually increased, until the patient died on the evening of the day after operation.

Necropsy Observations.—When the sternum with the attached costal cartilages was removed, the appearance of the lungs and mediastinal structures was striking. The pericardial cavity was moved over to the left side, the right side of the pericardium lying in the midsternal line. The apex of the heart was at the fifth interspace, 11 cm. to the left of the midsternal line.

Only a small margin of the lower border of the left lung was visible, this being of a purplish red. The upper lobe of the left lung was voluminous, and its color varied from bluish gray to pink. The right lung did not show any marked change, but its color was similar to that of the upper lobe of the left lung. The pleural cavities were free from fluid. The parietal and visceral pleura was clean and glistening, as was the pleural covering of the lower lobe of the left lung. The larynx, trachea, lungs and heart were removed together, with the least possible manipulation. The posterior surface of the trachea was then opened, and the mucosa of the trachea and of the bronchi was examined. The blood vessels of the mucosa of the trachea were injected. Considerable frothy, adherent but not tenacious mucus was attached to the lining of the trachea and bronchi of the first division. No obstruction in the form of a mucus plug, foreign body or collapse of the walls of the bronchi could be found. There was a marked

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difference in the size of the two lobes of the left lung, the upper lobe being voluminous; the lower lobe, flabby, a dark purplish red, and airless. The pleura covering the lower lobe was clean and glistening. The upper lobe was crepitant throughout and in color varied from a pale bluish gray to pink. The interlobar surface of the upper lobes showed irregular, dark red patches distributed beneath the pleura. On section the cut surfaces of the lower lobe appeared dark red and moist, and the moist scrapings, which were not abundant, showed a faint tinge of blood. The upper lobe was clean. The weight of the left lung was 500 Gm., and that of the right, 400 Gm.

The pulmonary artery was opened *in situ*, and evidence of thrombus was not revealed on tracing the vessel to its finer divisions.

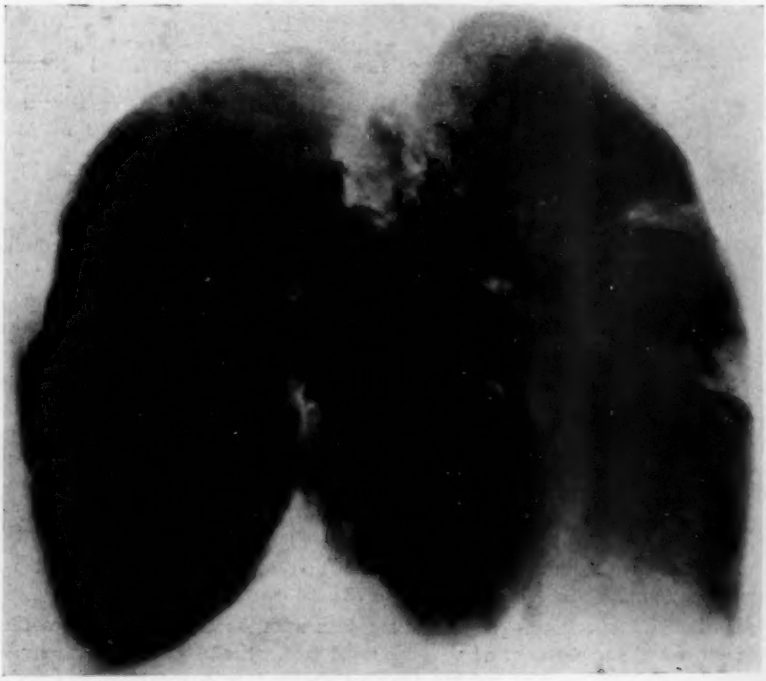

Fig. 2 (case 2).—Roentgenogram of specimen in a case of atelectasis following thyroidectomy. The increased density of the right lobe as compared with the left should be noted.

Examination of the larynx revealed an injury of the left recurrent laryngeal nerve.

A lesion of the heart was not found. The heart weighed 150 Gm. The myocardium was clean.

On microscopic examination, some of the alveoli were found to be collapsed. The majority of the alveoli contained mononuclear leukocytes, principally endothelial leukocytes, and lymphocytes. Some serum and red blood cells were present.

The bronchioles were clean. There was no thrombosis of the blood vessels.

The pathologic diagnosis was atelectasis of the lower lobe of the left lung.

Case 2.—A boy, aged 17 years, came to the clinic because of dyspnea on exertion, associated with hyperthyroidism and exophthalmos. The patient was

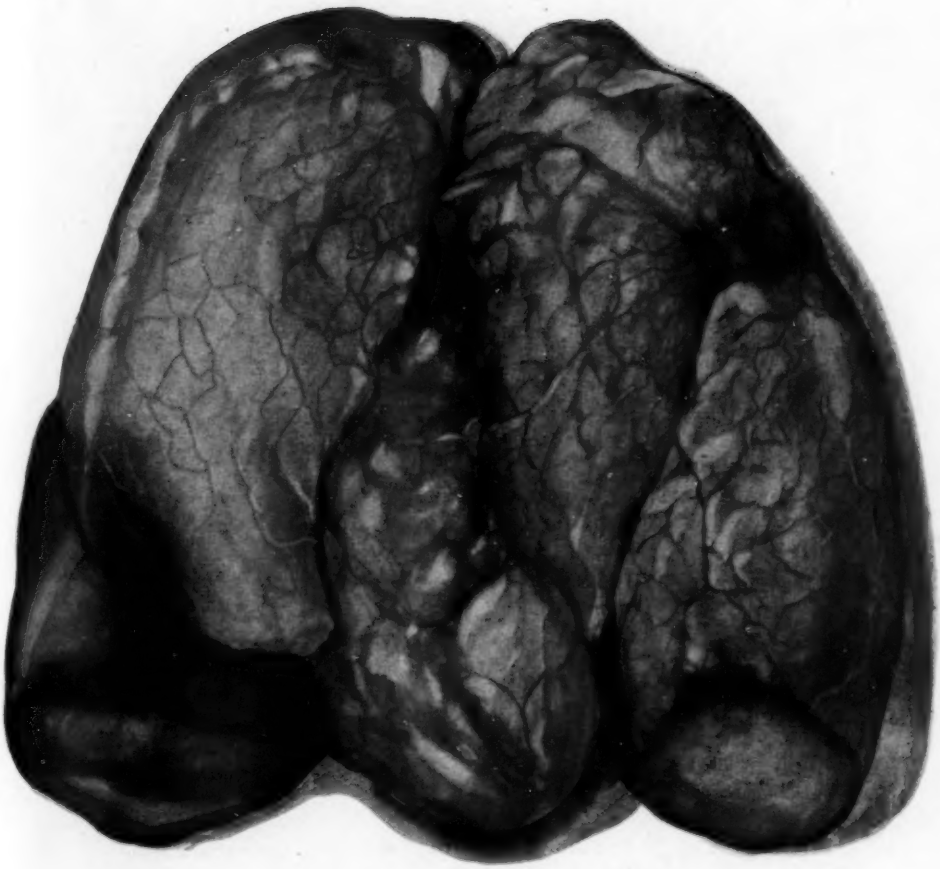

Fig. 1 (case 2).—Water color drawing of specimen in a case of atelectasis following thyroidectomy in which there was an anomaly of the lungs, atelectasis of the right lower lobe and persistent thymus.

sent home, where he was under the care of his family physician until November, 1926, when he returned to the clinic, showing no improvement and with increased dyspnea on exertion. Ligations were performed, and the patient again returned home. In March, 1927, he returned for lobectomy, and in April a right lobectomy was performed under local anesthesia and nitrous oxide-oxygen analgesia. During the operation a transient stridor was present, which became so alarming that a tracheotomy was performed. The opening made into the trachea was closed at

Fig. 3 (case 2).—Photomicrograph of atelectatic area in a case of atelectasis following thyroidectomy; × 75.

the end of the operation, at which time the patient was breathing easily and had a good voice. About six hours after the operation, the patient became cyanotic. The pulse rate was 160, respiratory rate 30 and temperature 104 F. The cyanosis was transient, but the pulse and respiratory rates remained rapid. On examination of the chest, the breath sounds on the right side over the lower lobe were found to be diminished. The respiratory excursion was about the same on both sides. The percussion note was resonant. The apex beat of the heart was well within the left nipple line. On the following night, the patient died.

Necropsy Observations.—When the sternum with the attached costal cartilages was removed, an anomalous position of the lungs was revealed. The right lung consisted of two lobes and the left of three. The lower lobe of the right lung was barely visible below the voluminous upper lobe, and it was a dark purplish red as compared with the upper lobe, the color of which varied from pale gray to pink. The position of the heart was bisected by the midsternal line. The thymus was large and extended to the atrioventricular junction (fig. 1).

Fig. 4 (case 2).—Photomicrograph of atelectatic area in a case of atelectasis following thyroidectomy. The mononuclear leukocytes, the serum and the red blood cells in the alveoli should be noted; × 75.

On removal, the left lung was found to present a uniform appearance throughout. The right lung weighed 800 Gm., the left 500 Gm. The lower lobe of the right lung was flabby and airless as contrasted with the crepitant upper lobe (fig. 2). On section, blood-stained, serous fluid was obtained from the cut surface of the lower lobe; while the upper lobe was pale gray and was moist (figs. 3 and 4).

The trachea and bronchi were clean, except for slight redness of the mucosa of the upper third of the trachea.

The pulmonary artery was opened *in situ*, and no evidence of thrombus or embolus was revealed.

The pathologic diagnosis was atelectasis of the lower lobe of the right lung; cardiac hypertrophy; anomaly of the lungs, and hypertrophy of the thymus.

CASE 3.—A white woman, aged 52, came to the clinic on June 28, 1927, complaining of nervousness, increasing worry over details and insomnia. She said that the thyroid gland had been large since she was 16 years of age. A diagnosis of colloid adenoma was made, and the patient was admitted to the Cleveland Clinic Hospital, where, after three days of preoperative care, a thyroidectomy was performed. There was inspiratory stridor during the operation. For five days the postoperative course was normal, but on the evening of the fifth day after operation the patient became cyanotic and had difficulty in breathing, and a tracheotomy was performed. Moist râles were heard at the base of each lung, and slight bilateral dulness to percussion was noted. The respiratory excursions were

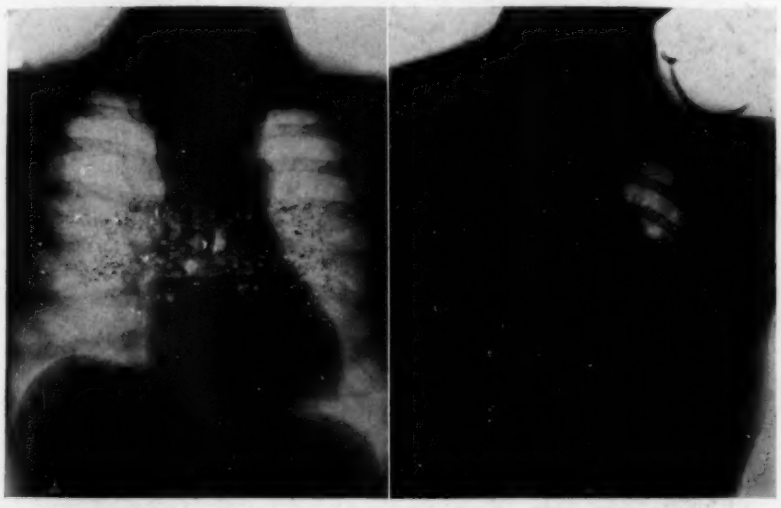

Fig. 5 (case 3).—Roentgenogram of lungs in a case of atelectasis following thyroidectomy; A—roentgenogram made on admission of patient to hospital and B—roentgenogram made after development of symptoms of atelectasis. The consolidation in the lower lobe of the left lung and in the middle and lower lobes of the right lung should be noted.

fairly good and symmetrical. The apex beat of the part was at the outer border of the left nipple line. A roentgenogram showed a dense shadow (consolidation) in the lower lobe of the left lung and in the middle and lower lobes of the right lung (fig. 5). The patient died fourteen hours after the tracheotomy.

Necropsy Observations.—When the sternum with the attached costal cartilages was removed, the heart and mediastinal structures were found to be in an apparently normal position. The apex of the heart was at the fifth costal interspace 10 cm. to the left of the midsternal line, and the right border of the heart was 3 cm. to the right of the midsternal line. The lower lobe of the left lung and the lower and middle lobes of the right lung were sharply differentiated from the upper lobes by the purplish red of the former, as contrasted with the bluish

pinkish gray of the upper lobes. The upper lobes were voluminous, and on the left side the upper lobe occupied considerably more space than the lower lobe, while on the right side the upper lobe occupied more space than both the lower lobes (fig. 6). An examination of the trachea and bronchi revealed an obstruction by mucus or a foreign body. The pulmonary arteries were free from emboli. Examination of the larynx revealed an injury to the left recurrent laryngeal nerve.

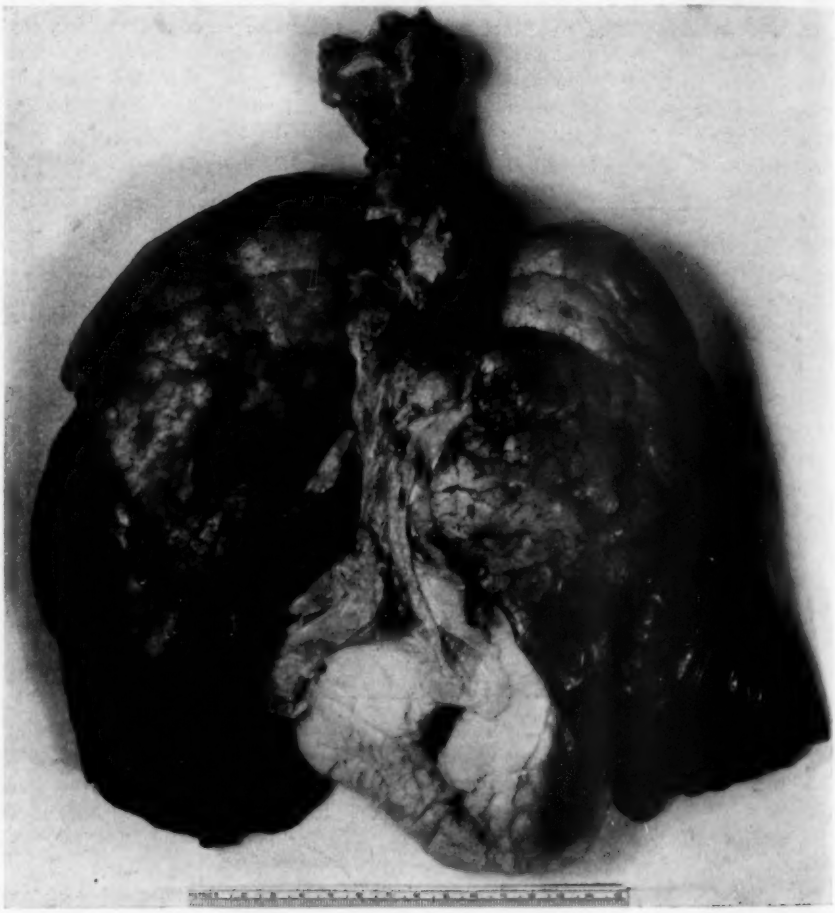

Fig. 6 (case 3).—Photograph of lungs, heart and larynx in a case of atelectasis following thyroidectomy. The relatively small size of the lower lobes should be noted.

The heart measured 12 mm. in diameter; it was clean, but the left ventricular wall was thickened.

The pathologic diagnosis was atelectasis of the lower lobes of both lungs and the middle lobe of the right lung; cardiac hypertrophy was present.

CASE 4.—A woman, aged 49, was admitted to the hospital with a diagnosis of adenomatous goiter with hyperthyroidism. She had lost 25 pounds (11.3 Kg.)

during the preceding four months. After twelve days of preoperative care, thyroidectomy was performed. Bilateral paralysis of the vocal cords followed the operation. Forty-eight hours later, a tracheotomy was performed because of the difficulty in breathing and the cyanosis. An examination of the chest showed moist râles on both sides. The respiratory excursion was fair and was about equal on the two sides. There was a bilateral resonant percussion note. The apex beat of the heart was at the left nipple line. The cyanosis, rapid breathing and fast pulse continued after the tracheotomy. Sixty hours after thyroidectomy the patient died.

Necropsy (Dr. Gay).—The pleura appeared clean and glistening; there was no deviation of the mediastinum. The pericardium was clean. The heart was in a state of dilatation, the apex being at the level of the fifth rib, 10 cm. to the left of the midsternum. The right border of the heart was 3 cm. to the right of the midsternal line.

The lungs with the heart and the larynx were removed in toto. The lower lobes of both lungs were of a dull purplish red. They were flabby and airless, and when viewed anteriorly, only a small margin near the base was visible. The upper lobe of the left lung and the remaining two lobes of the right lung were pinkish gray and crepitant. Dense fibrous adhesions united the interlobar surfaces of the upper and middle lobes of the right lung. On section of the lower lobes, a small amount of blood-stained serous exudate accumulated on the knife blade. The cut surface of the upper lobes was pale gray and moist. The pleural covering was clean.

No foreign body was found in the bronchi, but some frothy mucus was present. The coronary artery did not show any gross changes. Examination of the larynx revealed an injury of the recurrent laryngeal nerves.

The pathologic diagnosis was atelectasis of the lower lobes of the lungs and cardiac hypertrophy.

REVIEW OF LITERATURE

Atelectasis of the lungs has attracted the attention of pathologists and clinicians from the earliest times. The first references to this condition which appear in the literature are discussions of the reliability of the "sink or float" test of a lung in determining whether or not an infant had died in utero. In 1690, Schreyer [1] questioned whether or not the fact that the lung of a new-born child sank in water was proof that the child had died in utero. In 1728, Sailer [2] stated positively that this test was infallible. Croesser [3] and Camper [4] wrote articles on the treatment

1. Schreyer, J.: Erörterung und Erläuterung der Frage: Ob es ein gewiss Zeichen wenn eines todten Kindes Lunge im Wasser untersincket, dass solches in Mutter-Leibe gestorben sey? Zeitz, 1690.

2. Sailer, C. W.: De pulmonum subsidentium experimenti prudenti applicatione, Halae Magdeb., 1728.

3. Croeser, J. H.: Nader betogend berigt der betekenis van een dryvende en zinkende long van eerst geboren kinders, op en in het water, uit welk teken op sigh selfs genoomen, niet anders met sekerheid kan beslooten worden, als dat sso een kind, welkers long op het water dryft, gerespireered, en vervolgens in of na de geboorte geleeft heeft, etc., Groningen, 1741.

4. Camper, P.: Gerechtelyke en ontleedkundige Verhandeling over de tekenen van Leven, en dood in nieuwgeborene Kinderen, Leeuarden, 1774.

of patients with atelectasis, emphasizing the value of immersion of newborn children in water.

In 1876, Dr. Pearson Irvine [5] reported to the Clinical Society of London a case of diphtheria which was accompanied by progressive paralysis and marked symptoms in the upper lobes of the lungs. The patient, a young girl, recovered. Dr. Irvine stated that he thought the râles heard in the upper lobe, the dulness and the other symptoms of disease of the lung had been due to changes in the lung which had resulted from the paralysis of the muscles of respiration. In 1887, William Pasteur [6] reported a similar case, drawing the same conclusions as Irvine. Later, Pasteur had the opportunity to observe other cases of diphtheria associated with respiratory paralysis and performed necropsies in the fatal cases.[7] Pasteur's further studies of atelectasis are reported in the Bradshaw Lecture [8] of 1908, in which he calls attention to the occurrence of pulmonary atelectasis after operative procedures. In this lecture, he begins a discussion of the mechanism whereby this lesion is produced which was continued in later papers, with the addition of numerous case reports and some experimental work, notably that by Elliott and Dingley,[9] Scrimger [10] and Briscoe.[11] As has been reported by Bradford,[12] during the World War a number of atelectatic lungs were observed after traumatic injuries to various parts of the body had occurred. In 1924, Scott [13] found sixty-four cases on record in which atelectasis had followed operative procedures. Fifty cases were reported recently from one hospital as having occurred within a period of three months (Mastics, Spittler and McNamee).[14]

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5. Irvine, Pearson: Case Report to Clinical Society of London, Lancet **1**: 888, 1876.

6. Pasteur, W.: Paralysis of the Diaphragm After Diphtheria, with Extensive Pulmonary Collapse; Recovery, Lancet **1**:975, 1887.

7. Pasteur, W.: Respiratory Paralysis After Diphtheria as a Cause of Pulmonary Complications, with Suggestions as to Treatment, Am. J. M. Sc. **100**: 242, 1890.

8. Pasteur, W.: Massive Collapse of the Lung, Bradshaw Lecture, Lancet **2**:1351, 1908.

9. Elliott, T. R., and Dingley, L. A.: Massive Collapse of the Lungs Following Abdominal Operations, Lancet **1**:1305, 1914.

10. Scrimger, F. A. C.: Postoperative Massive Collapse of the Lung, Surg. Gynec. Obst. **32**:486 (June) 1921.

11. Briscoe, J. C.: Mechanism of Postoperative Massive Collapse in Lungs, Quart. J. Med. **13**:290, 1920.

12. Bradford, J. R.: Massive Collapse of Lung, Quart. J. Med. **12**:127, 1919.

13. Scott, W. J. M.: Postoperative Massive Collapse of Lung, Arch. Surg. **10**:73 (Jan.) 1925.

14. Mastics, E. A.; Spittler, F. A., and McNamee, E. P.: Postoperative Pulmonary Atelectasis, Arch. Surg. **15**:155 (Aug.) 1927.

ETIOLOGY

Physiologically, the lung is kept in a state of distention (1) by negative intrapleural pressure and (2) by positive intra-alveolar pressure. The alveolar walls cannot approximate each other unless both of these factors are diminished. A partial collapse will result if the intrapleural pressure is equalized with the pressure outside the pleural cavity. It does not always follow, however, that a partial collapse will occur if the intra-alveolar pressure is decreased for but a relatively short period of time, as was the case in two experiments on dogs which are to be reported in detail later. In considering the etiology of postoperative collapse, it is understood that the intrapleural negative pressure remains fairly constant. The deviation of the mediastinum to the affected side would prove that this is the case. The most probable single factor in changing the intra-alveolar pressure is an obstruction of the bronchus or of a bronchiole which supplies the atelectatic area. This obstruction may be mechanical or neurogenic in origin. If mechanical, it might be a foreign body, a plug of mucus, or pressure from an adjacent tumor mass (Junghagen).[15] If neurogenic, it could be a spasm of a bronchiole, a reaction similar to anaphylaxis, or angioneurotic edema.

That spasm of a bronchiole is an improbable cause of atelectasis is suggested by the high incidence of asthma, of which atelectasis is not a common complication. The spasm of the bronchioles in asthma is usually interpreted as arising from fibers of the vagus nerve (Pottenger),[16] and this is of great importance because of the association of atelectasis with injuries of the recurrent laryngeal nerve, as in the four cases here reported. It is doubtful whether a reflex irritation or spasm by itself alone could be responsible for atelectasis. That a condition resembling angioneurotic edema could cause atelectasis has been suggested by Bergmanini and Shepard,[17] who found the entire lungs to be edematous in two fatal cases in which death occurred during anesthesia.

That complete obstruction can cause atelectasis of the lung has been directly observed numerous times by Jackson,[18] in some of whose cases the atelectasis cleared up after the foreign body was removed. But in cases of atelectasis in which a foreign body or other mechanical obstruction is not present, it is obvious that some other cause must be responsible.

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15. Junghagen, S.: Some Cases of Pulmonary Atelectasis, Acta radiol. **5**: 250, 1926.

16. Pottenger, F. M.: Motor, Sensory and Trophic Reflexes from Lung, and Nerve Paths Through Which They Are Expressed, Am. Rev. Tuberc. **15**:477 (April) 1927.

17. Bergamini, H., and Shepard, L. A.: Bilateral Atelectasis (Massive Collapse) of Lung, Ann. Surg. **86**:25 (July) 1927.

18. Jackson, C., and Lee, W. E.: Acute Massive Collapse of the Lungs, Ann. Surg. **82**:364, 1925.

The mechanics of respiration have been described by Keith,[19] who calls attention to the three anatomic zones of the lung: "(*a*) The root, practically non-extensible; (*b*) the intermediate zone, containing vascular and bronchial ramifications with some extensible tissue between; and (*c*) the outer zone, consisting entirely of expansile tissue. Expansion takes place by the moving apart of the rays of the inexpansile structure, and the filling out of the intermediate and outer expansile areas." Keith has likened this to the opening of a Japanese fan. Soltau [20] also calls attention to the conical shape of the chest from the first to the fifth rib and to the cylindrical form from the fifth rib downward. The expansion of the upper lobes is mainly due to the action of the scaleni and intercostal muscles, the diaphragm not entering much, if at all, into the action. The lower lobes expand as the result of the action of intercostal muscles and of the diaphragm. Complete paralysis of the diaphragm is compatible with life (Scott)[13] as long as the intercostals and the accessory muscles of respiration are functioning.

It would appear that the most constant factor responsible for atelectasis is a lack of expansion of the lung, associated with some involvement of the respiratory tract which interferes with the normal intra-alveolar pressure. This interference with pressure might be brought about (*1*) by total or partial obstruction due to a foreign body or a plug of mucus (Elliot and Dingley),[9] (*2*) by a continued prolonged expiration with short shallow inspiration, as in deep anesthesia and often during the early stages of ether anesthesia, (*3*) by injury of the recurrent laryngeal nerves or (*4*) by tracheotomy, after which the normal resistance of the air is absent.

I believe the two last factors were mainly responsible for the atelectasis in the series of cases that I have reported. In such cases it would appear that when there is practically complete emptying of the alveoli in the lower lobe, due to the strong unresisted expiration and shallow inspiration, the intra-alveolar pressure is lowered with resultant edema or diapedesis, and in consequence the lobe becomes atelectatic. This conception is further substantiated by the frequent occurrence of the lesion on the right side, where the bronchi are larger than on the left. This is merely a conjecture, however, and has not been definitely proved, and the experimental work done on two dogs would indicate that it is not true. In my experiments, however, there was no limitation of respiratory movement, and moreover, dogs are not satisfactory animals for this experiment because of the occasional communication of the pleural cavities and the great mobility of the mediastinum.

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19. Keith, quoted by Soltau, Brit. M. J. **1**:544 (March 21) 1925.

20. Soltau, A.: Massive Pulmonary Collapse, Brit. M. J. **1**:544 (March 21) 1925.

CLINICAL SIGNS AND SYMPTOMS

The severity of the symptoms of atelectasis varies greatly, as it depends on the amount of involvement of the lung and on the cardiac reserve. The period of onset varies from one to six days, although the condition may be latent. There is usually elevation in temperature and rapid breathing, and often cyanosis (Eades).[21] The breath sounds are usually present on the affected side and are moist, but later in the disease they are diminished. Vocal fremitus may be present or absent. A mild or severe cough may be present. The mobility of the walls of the chest may be the same on the two sides.

Roentgenologic examination reveals a dense shadow of the affected area with a displacement of the heart and mediastinum toward the affected side when the condition is unilateral. In some cases, the diaphragm is fixed, but in others it moves normally. Usually lysis and reexpansion occur, but sometimes death supervenes or pneumonia may develop (Pasteur).[7]

PATHOLOGIC CHANGES

The pathologic observations in cases of atelectatic lungs are familiar to any one who has performed a number of autopsies. The observations in cases of postoperative lobar atelectasis without a demonstrable cause are similar to those in cases in which the cause is demonstrable. It differs mainly from lobar pneumonia or cases in which the lungs are compressed from without by the sharp limitation to one lobe and by the small shrunken size of the lobe. The alveolar walls are not always compressed together, but sometimes contain serum, red blood cells and mononuclear leukocytes.

The gross appearance is usually striking because of the relative difference in the size of the lobes. The atelectatic lobe is smaller and when in situ the lower lobe is almost completely hidden by the compensatory emphysematous upper lobe. The line of demarcation is fairly well marked, although there is some involvement of the interlobar surface of the adjacent lobe. A narrow zone of tissue at the upper border of the affected lobe may contain air, but the rest of the affected lobe is flabby, limp (Lee)[22] or pasty and airless. It is a dark purplish red, and the overlying pleura is clean and glistening. The cut surface is dark red, and when it is scraped, a serous exudate will accumulate. There is no dripping of serum as from the edematous lung found in cases of acute passive congestion or edema. When the cut surface is stretched in various directions, the movements of the alveolar walls are

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21. Eades, M. F.: Postoperative Massive Atelectasis, Boston M. & S. J. **195**: 258 (Aug.) 1926.

22. Lee, W. E.: Postoperative Pulmonary Complications, Ann. Surg. **79**: 506 (April) 1924.

seen—a further means of distinguishing this condition from inflammatory consolidation (MacCallum).[23]

On microscopic examination a few alveoli, the walls of which are in apposition, will be found, but most of the alveoli contain a cellular exudate which for the most part consists of mononuclear leukocytes, red blood cells and serum. "The lining epithelial cells of alveoli are prominent and more or less cuboidal in shape owing to contraction," as Mallory[24] has stated. The bronchi are clean. The blood vessels are tortuous and the veins are distended. Thrombotic blood vessels were not demonstrable in the cases here reported.

In most of the reported cases of postoperative atelectasis the condition has been complicated by pneumonia. This was naturally the case because of the infrequent deaths in uncomplicated cases. In the four cases reported here there was no demonstrable complication. The cause of death from atelectasis is uncertain. Because of the fact that the blood is circulating through the nonaerated lobe of the lung, there is an admixture of nonaerated with aerated blood and a deficient oxygenation of body tissues. This results in a greater demand on the heart, which in cases of hyperthyroidism is considered to have a low reserve. In such cases the demand is greater than the reserve.

SUMMARY AND CONCLUSIONS

Four fatal cases of lobar atelectasis are reported, two unilateral, two bilateral. In each case death followed an operation on the thyroid gland.

The pathologic observations were similar in each case. The atelectatic lobes were characteristic in appearance, presenting a disproportion in the size of the lobes, the atelectatic lobes being sharply demarcated by color, by a clean glistening pleura and by a flabby, limp consistency. The microscopic examination disclosed a picture not easily confused with any other lesion of the lung.

The etiology of these cases is apparently best explained on a mechanical basis, the most essentially responsible factor being a lowering of the intrapulmonary pressure.

In two incomplete experiments on dogs the intra-alveolar pressure was lowered without resulting atelectasis. Further experimental work is in progress and will be reported at a later date.

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23. MacCallum, W. G.: Textbook of Pathology, Philadelphia, W. B. Saunders Company, 1920, p. 414.

24. Mallory, F. B.: Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, 1923, p. 467.

A MALIGNANT RHABDOMYOMA OF SKELETAL MUSCLE *

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Rhabdomyomas of skeletal muscle are sufficiently rare to make the recording of each new example an obligation. Study of the case reported in this paper has revealed cytologic details of value in the recognition of rapidly growing rhabdomyomas and probably in the interpretation of the histogenesis of the myofibril. For the latter reason a more detailed study has been published in an anatomic journal.[1]

LITERATURE

The rarity of rhabdomyomas arising in skeletal muscle is indicated in the analysis by Küttner and Landois.[2] Of sixteen reported cases they accept ten as possible rhabdomyomas. In 1925 Abrikossoff [3] gives the number as eight. Comparison of the two articles shows that Abrikossoff included one case rejected by Küttner and Landois and added two cases reported since 1913. Abrikossoff added five cases of his own, three being rhabdomyomas of the tongue. Of the total of thirteen cases accepted by Abrikossoff, six occurred on the tongue. Three new cases of rhabdomyoma of the tongue have been reported since 1925. These are included in the recent paper by Dewey,[4] bringing the total of rhabdomyomas of the tongue to nine. Cases overlooked by Abrikossoff are that of Burgess,[5] a malignant rhabdomyoma with metastases apparently primary in the thigh; that of Reitter,[6] a rhabdomyoma of the nose; that of Nicory,[7] a rhabdomyoma of the uvula; that of Martin and Alexander,[8] a rhabdomyoma of the soft palate; that of Johanjun,[9] a "Rhabdomyosarcoma chondro-myxomatosum" of the upper arm, and that of Muller,[10] a rhabdomyosarcoma following successive fractures of the femur.

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* From the Department of Pathology of Harvard University Medical School and the Children's Hospital.

1. Wolbach, S. B.: Anat. Record, 1928, vol. 37.
2. Küttner, H., and Landois, F.: Deutsche Chirurgie, 1913.
3. Abrikossoff, A.: Virchows Arch. f. path. Anat. **260**:213, 1926.
4. Dewey, K. W.: Rhabdomyoma of the Tongue, Arch. Path. **3**:645 (March) 1927.
5. Burgess, A. M.: J. M. Research **29**:447, 1913-1914.
6. Reitter, G. S.: Rhabdomyoma of Nose, J. A. M. A. **76**:22 (Jan. 1) 1921.
7. Nicory, C.: Brit. J. Surg. **2**:218, 1923-1924.
8. Martin, G. E., and Alexander, W. A.: J. Laryng. & Otol. **39**:312, 1924.
9. Johanjun, B.: Frankfurt. Ztschr. f. Path. **22**:50, 1919.
10. Muller, H. R.: J. Cancer Research **2**:393, 1917.

Abrikossoff probably was too severe in his judgment of the cases accepted by Küttner and Landois. According to their judgment the total number of skeletal rhabdomyomas recorded would be twenty-seven instead of twenty-two, as would be true if one started with Abrikossoff's paper; the case recorded here is either the twenty-third or the twenty-eighth.

Earlier publications important from the casuistic aspect are those by Wolfensberger [11] in 1894 and by Benenati [12] in 1903. Wolfensberger lists sixty-three rhabdomyomas: thirty-eight of the urogenital system; five of the myocardium; four of the orbit and adjacent region; seven of the neck, possibly of thymus and pituitary origin, and nine of miscellaneous origin. Benenati tabulates sixty-four cases divided as follows: thirty-nine of the urogenital system; eight of the heart; one of the tongue; one of the orbit; and fifteen of miscellaneous origin, as follows, shoulder, tibia, mamma, anus, back, pectoralis major, nose, anterior mediastinum, femur, parotid, ischial tuberosity, hip, neck, esophagus and temporal region.

It is evident that rhabdomyomas arising in or adjacent to the urogenital system are the most common. Additional instances of rhabdomyoma, since Benenati's paper, exclusive of those arising in heart and skeletal muscle are: one occurring in the lung; [13] and six found in the urogenital system, including one in the uterus,[14] two in the vagina,[15] one in the ovary,[16] one in the interrenal region [17] and one in the testis.[18]

The literature concerning rhabdomyoma of the heart is more easily accessible. In 1907, Wolbach [19] tabulated twelve cases and in 1925 Uehlinger [20] collected a total of thirty-seven instances of solitary tumors and thirty of multiple tumors.

This cursory treatment of the literature is sufficient to indicate the difficulties attending an effort to be exacting in nomenclature and grouping of tumors of striated muscle, a task which has been shirked. I have paid attention to the microscopic descriptions in each case recorded and believed that the details here described in the early

11. Wolfensberger, R.: Beitr. z. path. Anat. u. z. allg. Pathol. **15**:491, 1894.
12. Benenati: Virchows Arch. f. path. Anat. **171**:418, 1903.
13. Zipkin, R.: Virchows Arch. f. path. Anat. **187**:244, 1907.
14. Robertson, A. R.: J. M. Research **20**:297, 1909.
15. Miller, C. J., and Gurd, F. B.: Surg. Gynec. Obst. **40**:391, 1910. Lockwood, C. D.: Rhabdomyosarcoma of Vulvar Orifice in Children; Report of Case, Arch. Surg. **14**:860 (April) 1927.
16. Hinwich, H. E.: J. Cancer Research **5**:225, 1920.
17. Gordon, W. H., and Feldman, M. S.: Ann. Clin. Med. **3**:706, 1925.
18. Sabrazès and Peyron: Compt. rend. Soc. de biol. **92**:617, 1925.
19. Wolbach, S. B.: J. M. Research **16**:495, 1907.
20. Uehlinger, E.: Virchows Arch. f. path. Anat. **258**:719, 1925.

differentiation of the tumor cells are new and will be of service in the identification of a group of tumors of skeletal muscle hitherto not recognized as of myoblastic origin.

REPORT OF CASE

History.—A girl, aged 4 years, with a tumor mass over the fifth and sixth dorsal vertebrae and symptoms pointing to pressure on the cord at this level, was admitted to the Children's Hospital, March 31, 1918. She was a full term infant, delivered normally; she was breast fed for ten months and was normal and well until the present illness.

For six weeks prior to admission her health was poor, without definite symptoms. During the ten days before entrance to the hospital she complained of attacks of pain in the abdomen which lasted from ten to fifteen minutes and occurred usually at night. There was no vomiting. She also had spells of itching at night which provoked violent scratching over the middorsal region. The attending physician did not consider her illness important and treated her for indigestion.

Examination and Course.—The child was well developed and nourished without the appearance of illness. She resisted examination, behaved rather hysterically, and would not stand without assistance, but did not seem to be in pain. The head, eyes, ears, nose, throat, chest and abdomen were entirely normal. On the back, a mass was found over the spine at the level of the fifth and sixth dorsal vertebrae. It was not tender and did not fluctuate; it was firm, and not adherent to the skin, but seemed connected to the spinal column.

Few neurologic observations were recorded. Examination of the extremities was difficult. The knee jerks were obtained. Kernig's sign and Babinski's sign were absent. Clonus was not demonstrated. Examinations of the blood and urine gave negative results. Later, on April 6, the child was irritable; otherwise she was drowsy and seemed mentally abnormal. She would neither sit up nor stand—the difficulty seemed to be one of balance rather than muscular weakness. Both knee jerks were hyperactive, and Babinski's sign was now present on both sides, with definite clonus on the left. On April 10 the patient was seen by a neurologist who made a diagnosis of probable tumor of the spinal cord at the level of the sixth vertebra. His objective observations were not recorded. On April 12 a laminectomy was performed. An infiltrating tumor pressing on the cord was found. This tumor extended through the intervertebral spaces and was continuous with the mass involving the spinal musculature. On May 3 the child was discharged unimproved. Further details of the progress of the tumor were not obtainable. The child died at her home on August 3.

The clinical history and description of the observations at operation leave much to be desired. The surgeon's impression was that the tumor was intraspinal in origin; yet a large growth existed in the spinal muscles, and, in view of the nature of the tumor, it is much more probable that its origin was in the muscles of the back and that it extended by way of the intervertebral spaces into the spinal canal.

A piece of tissue weighing approximately 1 Gm. and resembling voluntary muscle infiltrated with tumor was submitted to the pathologist.

History.—All the material was fixed in Zenker's fluid and embedded in three blocks. Sections from each block contained adult voluntary muscle fibers surrounded by tumor cells which in most fields had infiltrated between individual muscle fibers. The individual muscle fibers showed varying degrees of atrophy

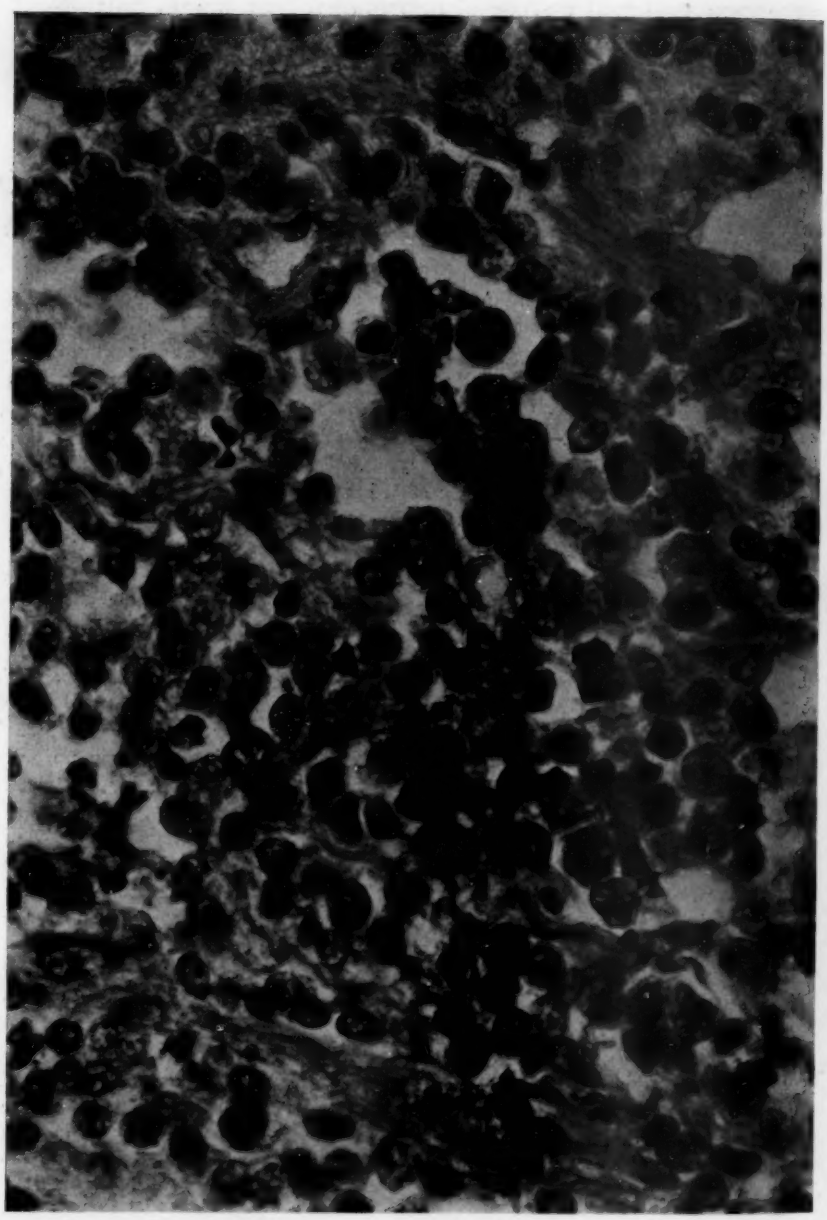

Fig. 1.—Photomicrograph at 700 diameters from section stained with hematoxylin and eosin, showing the round cells (myoblasts) of the least differentiated portions of the tumor.

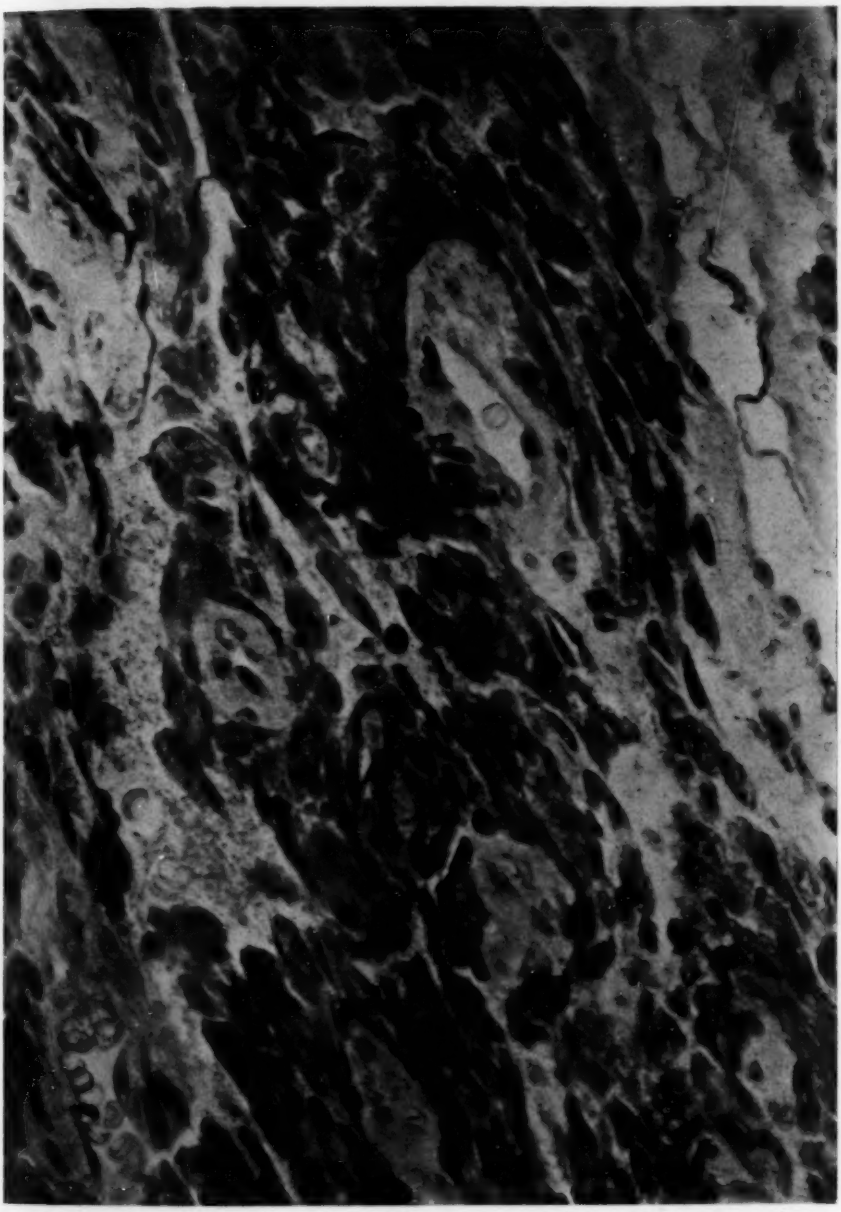

Fig. 2.—Photomicrograph at 700 diameters from section stained with hematoxylin and eosin, showing the fusiform and spindle shaped cells and their relation to the vascular stroma.

and degeneration, from normal appearing fibers to barely recognizable hyaline remains. There was no line of demarcation between an area of normal muscle of considerable size and the adjacent tumor. The first impression was that the growth was a sarcoma composed of round, spindle and polyhedral shaped cells actively invading skeletal muscle (figs. 1 and 2). This view was modified by the fact that where the tumor had wholly replaced the muscle there was a conspicuous accompaniment of compact fibrous connective tissue stroma; in some places it formed broad sheets enclosing nests of round tumor cells, and elsewhere it formed either large thick-walled alveoli lined and occasionally filled with tumor cells or fibrous cords, with central blood vessels, surrounded by tumor cells. When the last mentioned arrangement was found there was a further structural detail; cavernous blood-filled spaces were abundant and separated from one another the

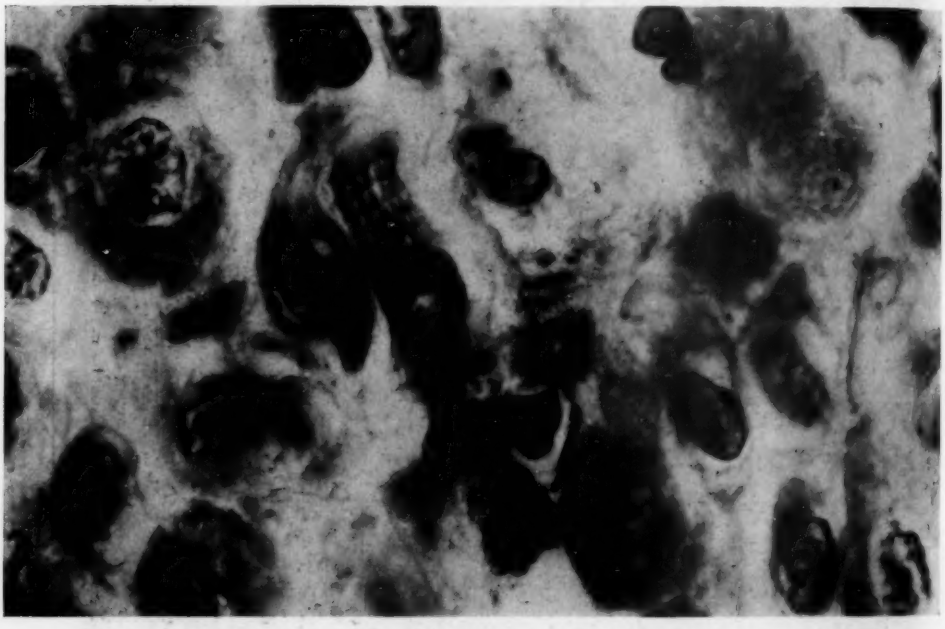

Fig. 3.—Photomicrograph at 2,000 diameters. A field containing one myoblast with orderly arranged granules connected by fibrils. The irregularity in the upper right hand group of granules — the junction of three small granules to one larger granule by fibrils — should be noted. The remaining cells contain granule clusters though but few are in the plane of focus.

units of vascular fibrous cords surrounded by tumor cells. The blood spaces were bounded by a single layer of endothelium; because of their irregular outline and invagination by tumor cells the appearance often suggested an intravascular growth of tumor.

The various forms of the stroma, particularly the broad, sheetlike type, often contained tumor cells, round and spindle shaped, in groups or evenly distributed among cells producing collagen, the latter arrangement suggesting a common origin of the connective tissue and tumor elements.

The recognition of the unusual architecture of the tumor led to a careful study of the cells which resulted in the observation of definitely cross-striated, spindle-

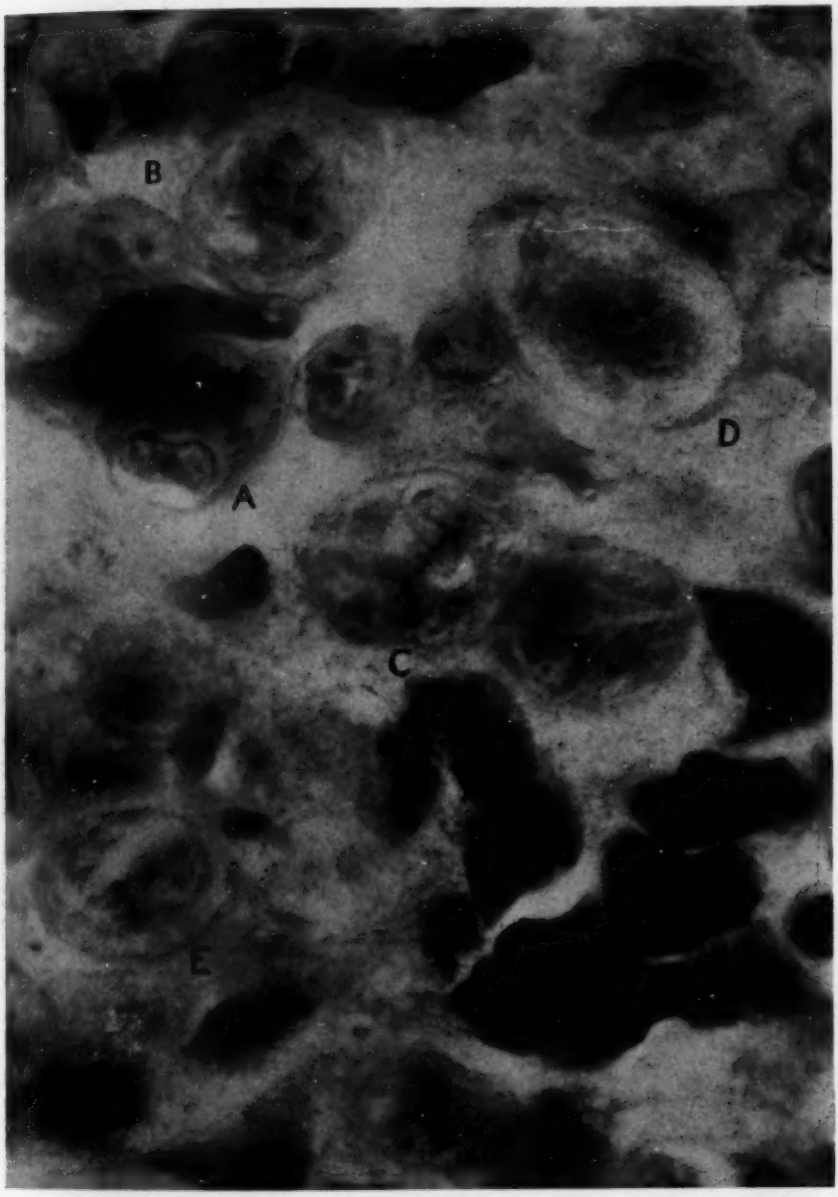

Fig. 4.—Photomicrograph at 2,000 diameters from section stained with Mallory's phosphotungstic acid hematoxylin. The myoblast at A contains a large group of centriole clusters without dispersion or fibril formation; at B and C, myoblasts with dispersed granules and fibril formation mostly in sheaf arrangement; at D, a cell with extremely minute granules and fibrils produced by fine division of centrioles without dispersion.

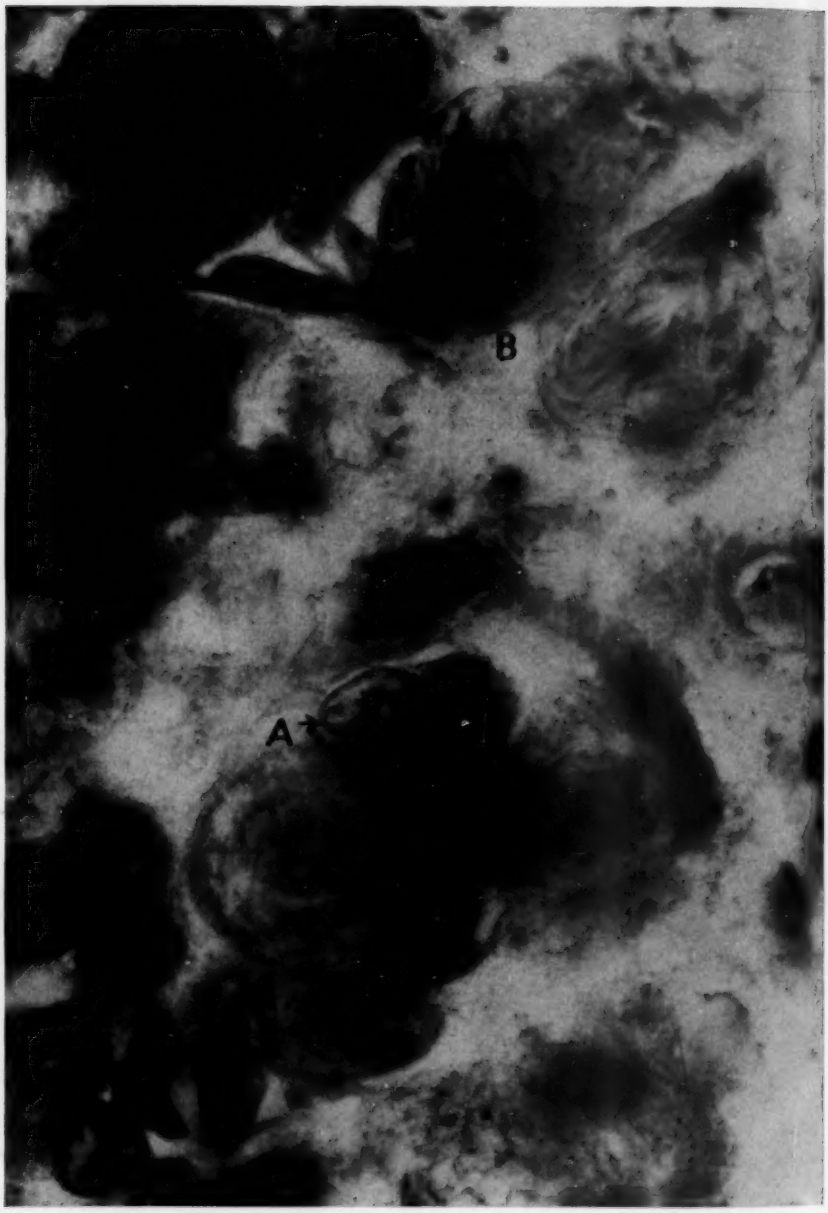

Fig. 5.—Photomicrograph at 2,000 diameters from section stained with Mallory's phosphotungstic acid hematoxylin. At A a myoblast with paired centrioles and early dispersion with fibril formation; at B granules and fibrils in formation suggesting multipolar mitosis.

shaped cells, and, hence, the knowledge that the tumor was a rhabdomyoma. Interesting details in the sequence of differentiation from undifferentiated to striated cells were subsequently found, and probably furnish important criteria for the recognition of rapidly growing tumors of myoblastic origin. Mallory's phosphotungstic acid hematoxylin was the most useful stain, and the descriptions are from sections so stained.

The most completely differentiated tumor cells were found in the regions with alveolar structure. Here, lining, and sometimes loosely filling, the alveoli formed by the stroma were definitely cross striated, spindle shaped cells. These cells had centrally placed nuclei and myofibrils; more often they showed only alternate broad and narrow bands, the former representing sarcomeres, the latter

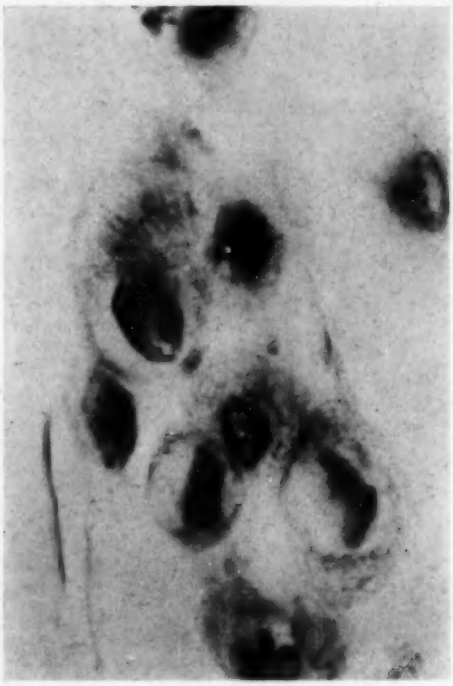

Fig. 6.—Photomicrograph at 2,000 diameters from section stained with Mallory's phosphotungstic acid hematoxylin. A myoblast with sheaf effect. The suggestion of binary division of the centrioles is shown.

the *Z* bands. Most frequently the striated appearance was produced by deeply stained blue granules strung on delicate brownish stained fibrils (fig. 3). In this instance the blue stained granules represented the sarcomeres, as careful study of the apparent sequences of development of the cells showed that these granules were the units which expanded into the sarcomeres. The brownish fibrillary material (which stained blue with Mallory's acid fuchsin aniline blue connective tissue stain) contracted and became the *Z* band material.

In less well differentiated parts of the tumor numerous mitotic figures were seen, and in the study of the sections special effort was made to find all appear-

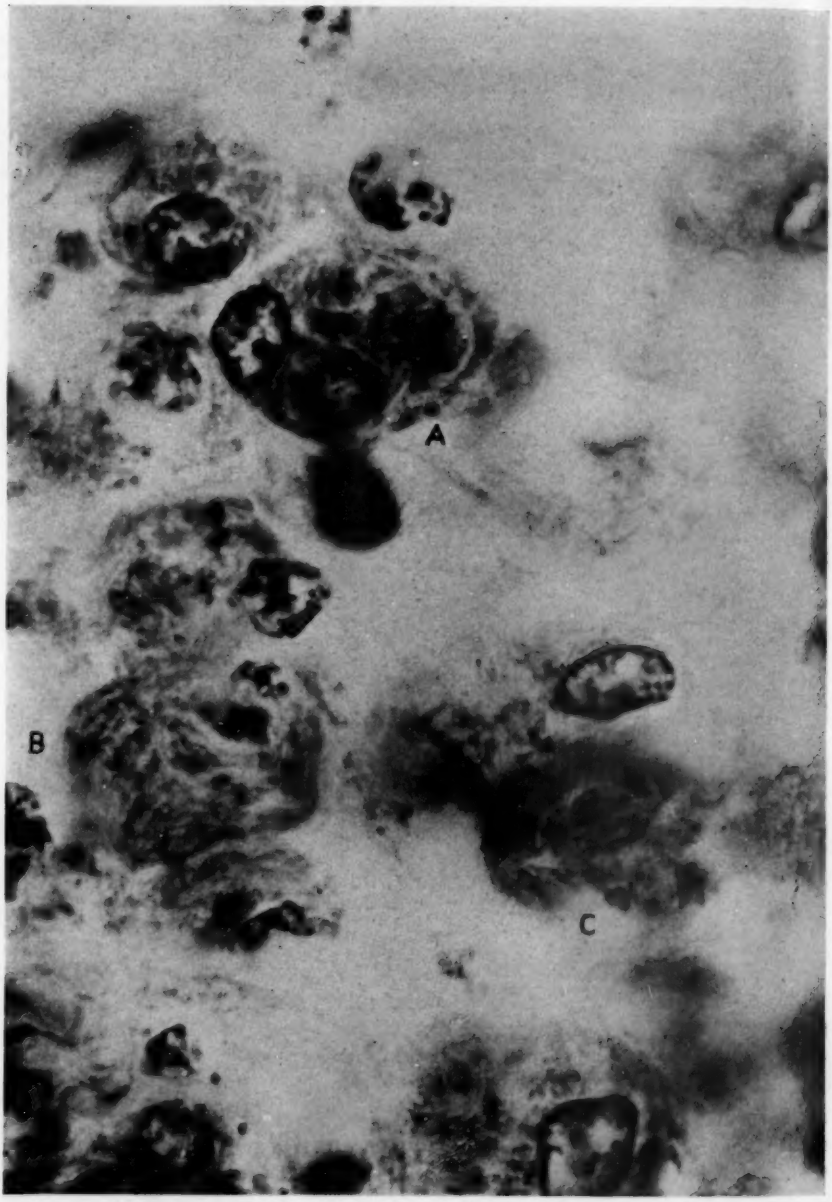

Fig. 7.—Photomicrograph at 2,000 diameters from section stained with Mallory's phosphotungstic acid hematoxylin. At A a myoblast with several systems of fibril formation, each probably the product of a centriole cluster; at B and C myoblasts with patterns produced by the irregular dispersion and division of the centrioles and subsequent fibril formation.

ances representing the intermediate stages of developmental sequences from the product of mitotic division to the cross striated cell.

Cells which with ordinary stains appeared to be of nondescript type, the polyhedral, round, oval and spindle cells invading muscle and distributed singly and in clusters in the fibrous tissue stroma, afforded with the phosphotungstic acid hematoxylin stain a variety of detail which could be assembled in apparent developmental sequence.

The simplest distinguishing feature found was the presence of clusters of paired centrioles in close proximity to the nucleus (figs. 4*A* and 5*A*). That the paired granules were centrioles was indicated by their size, staining reactions,

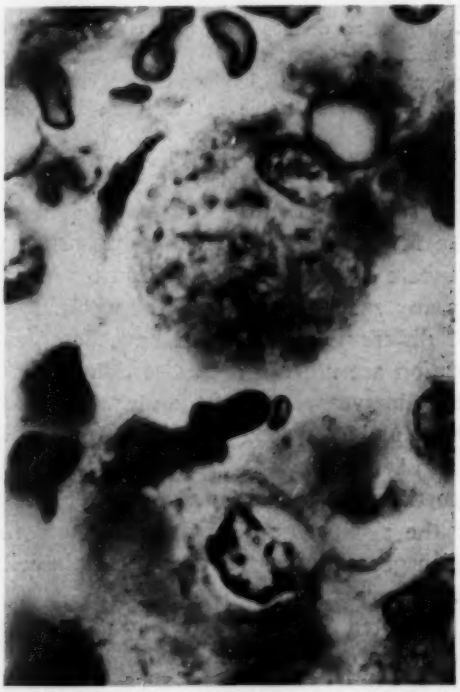

Fig. 8.—Photomicrograph at 2,000 diameters from section stained with Mallory's phosphotungstic acid hematoxylin. A myoblast with numerous sheaf like clusters of granules and fibrils. The fibrils connecting granules of different systems should be noted.

the surrounding clear zone and the presence of a material immediately surrounding them which corresponded to the centroplasm (Wilson[21]) or centrolinin (Heidenhain[22]). Next in complexity were the distribution of centriole clusters throughout the cytoplasm, and the appearance of delicate tapering fibrils extending in opposite directions from the granules (figs. 6, 4*B*, *C* and *E*, and 7*B* and *C*).

21. Wilson: The Cell in Development and Heredity, New York, The Macmillan Company, 1925.

22. Heidenhain, M.: Plasma und Zelle, in Bardeleben: Handbuch der Anatomie, Jena, 1911, vol. 8.

The granules (stained and measured from photomicrographs at 2,000 diameters) were approximately 0.2 microns in diameter. The fibril lengths measured from 3 to 5 microns or from granule to extremity from 1.5 to 2.5 microns.

Further complexity was found in increased numbers of granules and fibrils which were often arranged in bizarre groups—sheaflike, rosets, irregularly scattered granules connected by fibrils and in geometric patterns like those of multipolar mitoses (figs. 8, 5*B* and 7*A*). Cells with parallel fibrils and orderly arranged granules appeared occasionally, but such cells often showed irregularities such as one larger granule connected by fibrils to several smaller granules (fig. 3).

In following the stages of increasing complexity the appearances were such that one could not escape the conclusions that the granules divide by binary division in the axis of the fibril and separate in a direction transverse to the axis of fibril; and that the latter divides longitudinally and coincidently with the separation of the granules.

The fibril formation apparently took place at the expense of the cytoplasm, as the latter ceased to be demonstrable in the immediate vicinity of the fibril clusters or sheaves.

COMMENT

Because of the rarity of definitely cross-striated cells, this tumor corresponds to the few described as rhabdomyosarcoma and, probably owing to less fortunate circumstances of freshness of material, fixation and staining, to many sarcomas of skeletal muscle.

The details of differentiation which I have described as antecedent to myofibril formation are not recorded elsewhere. Robertson [14] in his description of a rhabdomyosarcoma of the uterus mentioned granules in orderly arrangement and described round and oval cells which in all probability might have revealed the details under consideration; Burgess,[5] in reporting a probable primary metastasizing malignant rhabdomyoma of the skeletal muscles described and illustrated round and oval cells, which grossly corresponded to certain cells (fig. 8 *D*) of my tumor.

In another paper (cited previously) I suggested the central apparatus (centriole) as the origin of the myofibril.

From the study of the case presented here it is evident that tumors of myoblastic origin may be identified, in the absence of definitely cross-striated cells, by the presence of centriole clusters and abortive fibril formation such as I have described and as are illustrated in figures 4, 5, 7 and 8.

Figures 3 to 8 inclusive are photomicrographs at 2,000 diameters from sections stained with Mallory's phosphotungstic acid hematoxylin.

MOBILIZATION AND TRANSFER OF CLASMATOCYTES *

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NEW YORK

The idea that mononuclear cells, the term being used in its broadest sense, are concerned in immunity to streptococcic infections is one that has been present in the literature for a long time. It is only in recent years, however, that attention has been focused on this relationship and that a tendency has been apparent to consider the mononuclears rather than the polymorphonuclears as the body's defenses in infections due to the streptococcus.

The question of the connection between the chief types of mononuclears, namely, the monocytes of the blood and the clasmatocytes or histiocytes of the tissues and the serous cavities, is one on which much work has been done but on which a final decision has not been reached. Simpson [1] believed that the identity of the two has not been proved, although there is no doubt of their close relationship. That the monocytes of the blood may change into macrophages in vitro has been shown by Lewis and Lewis.[2] On the other hand, Sabin and Doan [3] found both monocytes and clasmatocytes normally in the blood. Carrel and Ebeling [4] demonstrated that macrophages of the tissue and monocytes of the blood, when kept under similar conditions in tissue cultures, become identical. They believed that the two forms are different functional states of the same cell.

The cells designated variously as tissue macrophages, histiocytes, rhagiocrine cells, or clasmatocytes are the ones chiefly concerned in the present study. These cells offer the advantage of being easily recognized in the tissues through their reaction to certain vital dyes, notably trypan blue. They thus form part of the reticulo-endothelial system, as defined by Aschoff [5] and Kiyono.[6]

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* From the Department of Bacteriology, College of Physicians and Surgeons, Columbia University.

1. Simpson, M. E.: J. M. Research **43**:77, 1922.
2. Lewis, W. H., and Lewis, M. R.: Transformation of White Blood Cells into Clasmatocytes, J. A. M. A. **84**:798 (March 14) 1925.
3. Sabin, F. R., and Doan, C. A.: J. Exper. Med. **43**:823, 1926.
4. Carrel, A., and Ebeling, A. H.: J. Exper. Med. **44**:285, 1926.
5. Aschoff, L.: Lectures on Pathology, New York, Paul B. Hoeber, 1924.
6. Kiyono, K.: Die Vitalekarminspeicherung, Jena, Fischer, 1914.

The origin of these cells in lesions is probably double: from the monocytes of the blood, by change of function, and from the cells already present in the connective tissues. Lang [7] was unable to confirm the conclusion of McJunkin [8] and of Foot,[9] originally arrived at by Mallory,[10] that the capillary endothelium has a part in the formation of macrophages in the tissues; and in tissue cultures, Maximow [11] showed that endothelium gives rise to typical fibroblasts but not to ameboid elements. The connotation in the term "endothelial leukocyte" may thus be incorrect; by whatever term designated, however, the cells themselves are undoubtedly identical with clasmatocytes. Lewis [12] believed that the monocytes of the blood alone are capable of hypertrophying and forming macrophages and that the lymphocytes are not transformed into these cells. On the other hand, Maximow [13] stated that, in vitro, small lymphocytes change first into macrophages and then into fibroblasts.

Erysipelas was apparently the first streptococcic infection in which macrophages were observed. Metchnikoff [14] found large numbers of these cells in the lesions of human erysipelas, but asserted that the active resistance was due to the microphages. He believed that the function of the former cells was to take up weakened or dead polymorphonuclears, rather than bacteria. Later, Salimbeni,[15] working under Metchnikoff's direction on lesions of the skin in horses immunized against the streptococcus, noted the presence of macrophages in the tissues of the diseased areas, but attributed the healing process to the intervention of the polymorphonuclear cells. The predominance of small mononuclear cells in erysipelatous lesions has been further emphasized by MacCallum.[16]

A similar relationship has been found for other types of streptococcic infection. Thus, Bordet,[17] Zangemeister and Gans,[18] Wallgren,[19]

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7. Lang, F. J.: Rôle of Endothelium in Production of Polyblasts in Inflammation, Arch. Path. **1**:41 (Jan.) 1926.
8. McJunkin, F. A.: Am. J. Anat. **25**:27, 1919.
9. Foot, N C.: J. M. Research **40**:353, 1919.
10. Mallory, F. B.: J. Exper. Med. **3**:611, 1898.
11. Maximow, A.: Klin. Wchnschr. **4**:1486, 1925.
12. Lewis, M. R.: Am. J. Path. **1**:91, 1925.
13. Maximow, A.: Proc. Soc. Exper. Biol. & Med. **24**:570, 1927.
14. Metchnikoff, E.: Virchows Arch. f. path. Anat. **107**:209, 1887.
15. Salimbeni, A. I.: Ann. de l'Inst. Pasteur **12**:192, 1898.
16. MacCallum, W. G.: Textbook of Pathology, ed. 2, Philadelphia, W. B. Saunders Co., 1920, p. 52.
17. Bordet, J.: Ann. de l'Inst. Pasteur **11**:177, 1897.
18. Zangemeister, W., and Gans, H.: München. med. Wchnschr. **52**:793 and 858, 1909.
19. Wallgren, A.: Beitr. z. path. Anat. u. z. allg. Path. **25**:206, 1899.

and Kanai [20] demonstrated that the chief cells taking part in the destruction of streptococci, both in the blood stream and in the peritoneum, are large mononuclears. More recently, Bass,[21] working on rabbits immunized by living streptococci injected intravenously, came to the conclusion that the immunity which his animals developed depends chiefly on the phagocytosis and digestion of the cocci by cells of the reticuloendothelial system (histiocytes, tissue macrophages and clasmatocytes). From further observations, he concluded that cells of the tissue macrophage type react to opsonized organisms as do the leukocytes. Cecil [22] and Rosenow and Ashby [23] showed the importance of macrophage cells in lesions of the joints and myocardial lesions due to streptococci, and the rôle of the fixed macrophages of the tissues has been emphasized in the studies of Hopkins and Parker,[24] Keyes [25] and Nagao.[26]

A great deal of information on the correlation between streptococcic infections and cells of the clasmatocyte type has been brought out by the researches of Gay with various collaborators. He showed [27] that by the injection of various substances into the pleural cavities of rabbits two types of exudate can be produced. Infusion broth or 1 per cent egg white calls out large numbers of clasmatocytes in twenty-four hours, while an exudate induced by whole egg white or aleuronat is predominantly polymorphonuclear in character at the same time interval. It was further shown that animals with pleural exudates of the first type are protected against many times the fatal dose of streptococci injected intrapleurally, while animals with large numbers of polymorphonouclear cells succumb to a fatal infection as readily or even more quickly than normal animals. Active immunization of the pleural cavity against streptococci is simultaneous with a definite increase in the number of clasmatocytes. It was also found that in cavities "prepared" by broth and infected, sterilization is coincident with a marked increase in the number of these cells.

The relationship between clasmatocytes and immunity to the streptococcus was further investigated in a study of the changes occurring in the tissues surrounding the pleural cavity.[28] It was shown here that

20. Kanai, S.: Verhandl. d. Japan, path. Gesell. **1**:126, 1919.

21. Bass, F.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **43**:269, 1925.

22. Cecil, R. H.: J. Exper. Med. **24**:739, 1916.

23. Rosenow, E. C., and Ashby, W.: Focal Infection and Elective Localization in Etiology of Myositis, Arch. Int. Med. **28**:274 (Sept.) 1921.

24. Hopkins, J. G., and Parker, J. T.: J. Exper. Med. **27**:1, 1918.

25. Keys, P.: J. Infect. Dis. **18**:277, 1916.

26. Nagao, K.: J. Infect. Dis. **27**:327, 1920.

27. Gay, F. P., and Morrison, L. F.: J. Infect. Dis. **33**:338, 1923.

28. Gay, F. P.; Clark, A. R., and Linton, R. W.: Histologic Basis for Local Resistance and Immunity to Streptococcus, Arch. Path. **1**:857 (June) 1926.

the character of the exudate reflects the condition of the subjacent tissues. A cavity, prepared seventy-two hours before infection by the injection of a mixture of gum arabic and beef extract, quickly becomes sterile; its walls are found to be thickened and filled with a granulation tissue. Many of the cells of this tissue are clasmatocytes, and in them organisms could be observed undergoing destruction. On the other hand, when the pleural walls have been acutely inflamed by the injection of aleuronat and starch eighteen hours previously and when they are filled with polymorphonuclear cells almost exclusively, the animals are without protection. The organisms quickly invade the inflamed areas; necrosis sets in, and death of the animal follows in four or five days. The phagocytosis of streptococci by polymorphonuclears is negligible in these tissues.

It thus appears from the work of Gay and his collaborators that there is a definite and constant correlation between clasmatocytes and resistance to streptococcic infections in the pleural cavities of rabbits.

The importance of macrophages of the tissues (clasmatocytes) in other bacterial infections has been emphasized by various workers. Thus, Buxton [29] concluded that the resistance of rabbits immunized against typhoid is dependent on the increased ability of the macrophages to destroy the organisms, and Jelin [30] showed that the blood of rabbits is rid of *B. typhosus* by means of cells of the macrophage type. By means of vital staining, Oliver [31] demonstrated that the lepra cell in leprosy in rats is derived from the histiocyte. A monocytosis in malaria, typhus fever and relapsing fever was reported by Kartaschawa [32] and in cholera by Netousek.[33] In kala-azar, Meleney [34] found that the body reacts to the parasite by the proliferation of the large mononuclear phagocytes of the connective tissues. These observations have been extended by Hu and Cash,[35] who stated that the typical lesions of this disease contain cells of the reticulo-endothelial system almost exclusively. It was further shown that this system is practically the only part of the body involved in the disease. Jungeblut [36] further emphasized the importance of a normal reticulo-endothelial system in protozoan infections and has suggested that chemotherapeutic substances which are inactive in vitro may owe their activity in vivo to the cells of this system.

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29. Buxton, B. N.: J. M. Research **16**:251, 1907.
30. Jelin, W.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **47**:199, 1926.
31. Oliver, J.: J. Exper. Med. **43**:233, 1926.
32. Kartaschawa, F. W.: Arch. f. klin. Med. **146**:226, 1925.
33. Netousek, M.: Folia haemat. **17**:407, 1913.
34. Meleney, H. E.: Am. J. Path. **1**:147, 1925.
35. Hu, C. H., and Cash, J. R.: Proc. Soc. Exper. Biol. & Med. **24**:469, 1927.
36. Jungeblut, C. W.: Ztschr. f. Hyg. u. Infektionkrankh. **107**:357, 1927.

More closely related to the work to be reported in the present paper are the results of Nakahara.[37] This author induced a macrophage reaction in the peritoneal cavity of mice by injecting olive oil. Coincident with this increase in macrophages, there occurs a local resistance to fatal doses of staphylococci and pneumococci as well as a quicker disposal of *Bacillus coli*. The resistance is due to phagocytosis of the organisms by the macrophages. When *Bacillus coli* is injected into the pleural cavities, however, it does not disappear any more rapidly in animals with a peritoneal exudate of macrophages than in the normal controls.

My purpose in the present study has been to determine the relationship between a focus of cells of known type in one part of an animal's body and an irritant, either animate or inanimate, in another part. Interest in this problem came from work reported elsewhere (Gay, Linton and Clark[38]) on the relations of immunity between the two pleural cavities. In these papers it was shown that the immunization of one cavity against a streptococcic infection, accomplished by the formation in its wall of a granulating tissue rich in clasmatocytes, is coincident with the immunization of the other cavity. The two cavities, while equally protected, differ histologically in that the untreated one is normal in appearance before infection. After it is irritated, however, large numbers of clasmatocytes quickly appear in its walls, and by means of vital staining it could be shown that at least part of these cells came from the focus on the opposite side.

In the present work the relationship between a focus of cells in the peritoneal cavity and irritants or streptococci in the pleural cavities has been particularly studied. The right cavity has always been used for the tests. The left cavity has served as a control in some of the experiments. The first part of the work deals with experiments in which the focus of cells was formed in the peritoneum, followed by the injection of aleuronat and starch in the right pleural cavity. In the second half of the work, streptococci were used as the intrapleural irritant, subsequent to the formation of a peritoneal focus of cells.

Rabbits weighing about 2,000 Gm. were used. Tissue was fixed in Zenker's fluid without acetic acid. Sections were cut at 8 microns and were stained with eosin and methylene blue, and with safranine alone as a counter stain for the trypan blue. The pieces used for embedding and sectioning were taken as nearly as possible from the same area in each animal, namely, between the sixth and seventh ribs in the pleural wall, and to the right of the midline and somewhat laterally in the peritoneum.

37. Nakahara, W.: J. Exper. Med. **42**:201, 1925.

38. Gay, F. P.; Linton, R. W., and Clark, A. R.: Proc. Soc. Exper. Biol. & Med. **24**:23, 1926; (footnote 28).

A part of the omentum was taken in many cases. It was prepared by being spread over a slide, allowed to dry in air, fixed for five minutes in absolute methyl alcohol, and finally stained with safranine or Wright's stain.

MOBILIZATION BY MEANS OF ALEURONAT AND STARCH

The following typical protocol illustrates the methods used in the first part of the work:

PROTOCOL A

Group A. 5 cc. of aleuronat and starch[39] injected intraperitoneally, first day
5 cc. of aleuronat and starch injected intraperitoneally, third day
5 cc. of aleuronat and starch injected intraperitoneally, fifth day
5 cc. of 1 per cent aqueous trypan blue[40] injected intraperitoneally, seventh day
3 cc. aleuronat and starch injected into the right pleural cavity, ninth day
Killed twelfth day

Controls:

Group B. 5 cc. of 1 per cent aqueous trypan blue injected intraperitoneally, seventh day
3 cc. aleuronat and starch injected into the right pleural cavity, ninth day
Killed twelfth day

Group C. 5 cc. of aleuronat and starch injected intraperitoneally, first day
5 cc. of aleuronat and starch injected intraperitoneally, third day
5 cc. of aleuronat and starch injected intraperitoneally, fifth day
5 cc. of 1 per cent aqueous trypan blue injected intraperitoneally, seventh day
Killed twelfth day

Group D. 5 cc. of 1 per cent aqueous trypan blue injected intraperitoneally, seventh day
Killed twelfth day

The three intraperitoneal injections of the aleuronat-starch mixture on alternate days were intended to irritate the serosal lining of this cavity and cause the formation of a granulating tissue, which would contain clasmatocytes. The presence of these cells was determined by the use of trypan blue. Histologically, the peritoneal walls of animals thus treated and killed on the twelfth day showed marked changes (fig. 1). The cells of the serosal lining were intact and swollen. The subserous changes were striking. Enormous numbers of clasmatocytes as well as numerous fibroblasts were present; the latter were distinguished from the former by the small amount of dye stored in their cytoplasm. Polymorphonuclears were relatively rare. New blood vessels had been

39. This is a mixture of 5 per cent aleuronat and 3 per cent starch.

40. The trypan blue (National Aniline & Chemical Works) is made up in distilled water, filtered and autoclaved for twenty minutes before use.

formed throughout, and in some sections bits of the irritant were found below the intact serosa. The thickness of the wall had been increased from approximately 30 microns to an average of 300 microns. The picture was thus that of a typical granulation tissue. The omentums from these cavities also showed a large increase in clasmatocytes.

The animals in group A were designated to test the possibility of "cell transfer" from the peritoneum to the right pleural cavity. Hence, a peritoneal focus of clasmatocytes was first formed by the injection of the aleuronat and starch mixture, and subsequently the right pleural cavity was irritated. The animals in the other three groups served in various ways to control the A group. Thus, animals in group B were

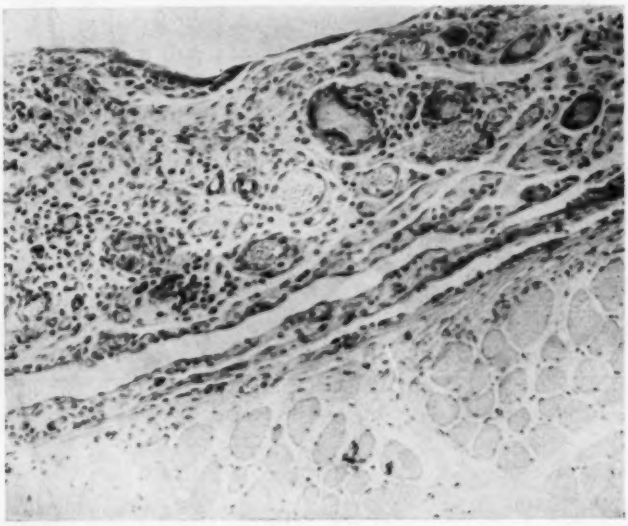

Fig. 1 (rabbit 5042).—Peritoneal serosa of a rabbit given three intraperitoneal injections of aleuronat-starch mixture. Large mass of granulation tissue, averaging 472 microns in width containing numerous clasmatocytes; × 120.

given dye in the peritoneum, which was otherwise untreated. They received the same amount of irritant in the pleural cavity and at the same time as the animals in group A and thus controlled the efficacy of the pleural irritant itself in causing changes in the serosae. Conversely, the animals in group C., in which dyed peritoneal foci were formed, tested the effect of these granulating areas on untreated pleural cavities. Group D, in which the animals were given a single intraperitoneal injection of dye, was designed to show the effect of trypan blue alone on the surfaces of the peritoneal and pleural cavities.

The character of the exudates, as well as their structure and composition, was studied since it had been shown elsewhere that it reflects the

condition of the underlying tissues. The results of these studies are shown in table 1. The most interesting contrast is that between groups A and B; that is, between animals with equally irritated pleural cavities, but differing in that the first contains a "peritoneal focus" of clasmatocytes. In respect to the amount of fluid in the right pleural cavity, the A group is slightly superior, about 3 cc. being present in comparison with 2 cc. in the animals that had not received peritoneal irritation; in the latter, however, the total number of cells is somewhat greater: from 254 to 211 million. But it is in the relationship between the cell types that the chief differences lie. In animals with merely irritated pleural cavities, the proportion between the average number of clasmatocytes and the average number of polymorphonuclears is 1:2.5, while in the group having a "peritoneal focus," the clasmatocytes are much higher,

TABLE 1.—*Summary of Studies of Exudates in the Right Pleural Cavities of Rabbits in Groups A, B, C and D*

	Amount Fluid, Cc.	Total Cells*	Total Clasmatocytes	Total Polymorphonuclears	Percentage Clasmatocytes	Percentage Polymorphonuclears	Percentage Trypan Blue	Total Trypan Blue Cells*
Group A (9)†...	3.2	211.0	129.3	81.6	60	40	4	1.3
Group B (5)....	2.1	254.0	74.0	180.0	30	70	10	7.5
Group C (3)....	0.1	0.4	0.35	0.048	88	12	0	0.0
Group D (3)....	0.01	0.28	0.25	0.019	92	8	11	0.034
Normal control	0.1	0.35	0.3	0.05	85	15	0	0.0

* In millions.
† The figures in parenthesis give the number of animals on which the averages are based.

the proportion being 1:0.5. Furthermore, there are about twice as many clasmatocytes in the right pleural cavities of animals in group A as in those in group B; that is, approximately 130 million in contrast to 74 million. If one expresses the values as percentages of the total white blood cells present in these exudates, animals without "peritoneal foci" show 30 per cent clasmatocytes, while animals with such granulating areas show 60 per cent clasmatocytes. In brief, the animals with a "peritoneal focus" of clasmatocytes show a decided superiority both in the relative and in the absolute numbers of these cells in their irritated pleural cavities.

The exudates of the peritoneal and left pleural cavities do not differ appreciably in the two groups, although here, too, the percentage of clasmatocytes is higher in the nonirritated left cavities of A than in B (80 per cent in contrast to 65 per cent). The exudates in group C are those of normal cavities. Accordingly, the peritoneal irritant itself does not affect the ratios or the totals of the cells in the pleurae, nor does the

peritoneal aggregation of cells cause any intrapleural changes. Likewise, in group D the dye did not change the proportion of cells to each other or their totals, and the exudates were normal.

HISTOLOGIC OBSERVATIONS

The normal serosal lining of the parietal and diaphragmatic pleurae, as well as that of the peritoneum, consists of a single layer of flat mesothelial cells. The subserosa, which lies between the mesothelial cells and the muscles, is formed of bundles of elastic fibers lying in various directions and interspersed with a few mononuclear cells, some of which by vital staining can be distinguished as tissue macrophages or clasmatocytes. Polymorphonuclear cells are rarely found.

When an irritant such as an aleuronat-starch mixture is injected into the pleural cavity, a typical inflammatory reaction develops in the serosal lining. The subserous and adjacent intramuscular capillaries become congested and from them large numbers of polymorphonuclear cells appear, and pass out into the cavity between the serosal cells. The latter are swollen and show some mitosis. Seventy-two hours after the injection of the irritant, the polymorphonuclears have practically disappeared from the subserosa; their place has been taken by macrophages and fibroblasts. In animals in which vital stains have been employed, many of the macrophages prove to be clasmatocytes. The serosal cells are rounded up and show much mitotic activity. In some cases they may form a layer two or three cells in thickness. In short, at this period, the acute inflammation has given way to a characteristically chronic condition with clasmatocytes as one of the chief components of the reaction.

The animals in groups A and B were killed seventy-two hours after the intrapleural injection of the irritant. The course of events already described was found to occur in both groups, and the character of the infiltration at this time in both was predominantly mononuclear. In this respect the presence of a large focus of clasmatocytes did not effect a difference in the two groups. The two groups do differ markedly, however, in the amount of thickening which their walls have undergone. This thickening is, in general, proportional to the number of cells which have infiltrated the area, but while it is due chiefly to cellular infiltration, two other factors play a part: the accumulation in the tissue of fluid, both in the lymph spaces and between the cells, and an increase in the number of connective tissue fibers. The number of mononuclears in the walls, as well as the amount of intercellular fluid, is generally greater in animals with a "peritoneal focus" than in animals with normal peritoneums. This fact also finds expression in the amount and character of the exudates in the two groups. As already pointed out, the amount

of pleural fluid in group A is about one-half larger than that in group B, while the number of clasmatocytes is twice as great. On the other hand, the fibers of the connective tissue vary irregularly. In some instances, they do not show any increase in number; in other animals, their number is somewhat larger than normal. There does not seem to be any constant relationship between them and the presence or absence of a peritoneal focus. In no case, however, is their variation from normal striking.

Table 2 gives the measurements, in microns, of the serosal linings of the various groups.[41] Each figure represents the average of several determinations of the distance from the muscles to the outer margin of the serosal cells. The right pleural wall of group A averages 177 microns or about six times the normal width, while the corresponding measurement in group B gives approximately four times the normal thickness. The most striking contrast, however, occurs in the pleural diaphragms of the two right cavities. Group B in this tissue shows a

TABLE 2.—*Summary of Measurements of Serosal Linings, in Microns*

			Right Diaphragm			Left Diaphragm	
	Peritoneal Wall	Right Pleural Wall	Peritoneal Wall	Pleural Cavity	Left Pleural Wall	Peritoneal Wall	Pleural Cavity
Group A.....	414	177	57	494	67	49	47
Group B.....	33	122	45	210	30	41	32
Group C.....	367	34	58	34	..	..	..
Group D.....	47	25	38	41	..	..	..
Normal control..	32	28	36	28	28	36	28

thickening of seven times normal, while the animals with a "peritoneal focus" (group A) show a serosal lining seventeen times normal in width.

The left cavities of these two groups show a smaller but still a clear-cut difference. Histologically, the superior thickening of the left cavities of the animals in group A is due entirely to an infiltration of monocytes. This change has not occurred in the other group in which the walls have remained normal.

The determinations in group C show that without irritation an effect is not produced in the right pleural wall or diaphragm of animals with a peritoneal focus. Similarly, the measurements of animals in group D are approximately normal throughout. In the last two groups the left cavities were not studied histologically, as it was assumed that they would not differ appreciably from the right cavities.

41. The measurements were made by means of a filar micrometer. Points above the trabeculae of the connective tissue were always avoided in making the determinations.

As would be expected from the figures, the cellular response to the irritant is found to be stronger histologically in the pleural diaphragm than in the pleural wall. This difference is particularly marked in group A. In the diaphragm, cords of mononuclears extend from the pleural surface down between the muscle bundles. In some instances this collection of monocytes in the tissues is marked as far down as the middle of the diaphragm. Many of these cells contain trypan blue; there does not seem to be a constant relationship between them and the capillaries. This intermuscular collection of mononuclears and clasmatocytes is present only to a slight degree in group B. Here the infiltrating cells tend to collect under the pleural serosa and extend into the muscles only a short distance. This difference in appearance and in the number of cells present does not come out in the serosal measurements, since distances below the muscles are not measured. A similar intermuscular collection of cells, also presumably from a distant focus, has been reported in transfer experiments between the right and left cavities (Gay, Clark and Linton [28]).

The parietal pleurae of the two groups resemble each other in general, with the exception of the number of cells which has appeared in each. Intermuscular cords of mononuclears are absent in both, although the trabeculae of the connective tissue may be crowded with cells for a short distance below the surface. The pleural surfaces of the wall and diaphragm are much more alike in group B than in group A.

Thus, under the conditions of these experiments, animals with "peritoneal foci" show in their irritated pleural cavities a marked superiority both in the number and proportion of clasmatocytes present over controls without such foci. Similarly, the serosal linings of their pleural walls and diaphragms show a decided increase in thickening in contrast to the controls. This thickening is due principally to infiltration by clasmatocytes. The distribution of cells containing trypan blue in these pleural cavities will be discussed later.

MOBILIZATION BY MEANS OF INTRAPLEURAL STREPTOCOCCIC INFECTION

The following protocols were used in this part of the work:

PROTOCOL B

Group 1. 5 cc. aleuronat and starch injected intraperitoneally, first day
5 cc. aleuronat and starch injected intraperitoneally, third day
5 cc. aleuronat and starch injected intraperitoneally, fifth day
From 100 to 250 times the minimum lethal dose of a twenty-four hour broth culture of passage fluid streptococcus "H" in 1 cc. amount injected intrapleurally into the right cavity, ninth day

Group 2. 5 cc. aleuronat and starch injected intraperitoneally, first day
5 cc. aleuronat and starch injected intraperitoneally, third day
5 cc. aleuronat and starch injected intraperitoneally, fifth day
5 cc. of 1 per cent aqueous trypan blue injected intraperitoneally, seventh day
From 100 to 250 times the minimum lethal dose of a twenty-four hour broth culture of passage fluid streptococcus "H" in 1 cc. amount injected intrapleurally into the right cavity, ninth day

Group 3. From 100 to 250 times the minimum lethal dose of a twenty-four hour broth culture of passage fluid streptococcus "H" injected intrapleurally into the right cavity, ninth day

Group 4. 5 cc. aleuronat and starch injected intraperitoneally, first day
5 cc. aleuronat and starch injected intraperitoneally, third day
5 cc. aleuronat and starch injected intraperitoneally, fifth day
5 cc. of 1 per cent aqueous trypan blue injected intraperitoneally, seventh day
Killed ninth day

In groups 1 and 2, the same methods for producing peritoneal granulating areas which had proved successful in the work already reported were employed.

The animals in group 1 differ only in that they were not given trypan blue intraperitoneally. Group 3 indicated the course of the intrapleural infection in normal animals. The rabbits in group 4 presented the condition of the pleural cavities at the time of infection; these animals had dyed "clasmatocyte foci" in their peritoneums, while their pleural cavities were untouched. They were killed at the same time that the animals of groups 1 and 2 were infected. The strain of streptococci used here is the same one which has been repeatedly described by Gay and his co-workers.[27] It was originally derived from a fatal human case of empyema, and its virulence for rabbits has been raised to a high degree by repeated passages through the pleural cavities of these animals at intervals of about one month. Between passages, it is kept in pleural fluid in the icebox. Approximately fifteen chains now constitute a minimal lethal dose. The accurate method of counting which has been developed is described elsewhere.[27]

Of the twenty-six animals infected and allowed to go on to death or recovery, twelve belonged to group 1 and fourteen to group 2. Of the entire number, seven animals, or 27 per cent died with typical pleural infections at the usual interval of four or five days. The controls in group 3 always died with typical infections. Intraperitoneal preparation thus gives a survival of 73 per cent of the infected animals. It is interesting to note that four of the seven unprotected animals had been treated with dye (group 2), while among the nineteen survivors only six had been so treated. If one expresses the values in percentages, 31 per

cent of the surviving animals had been given trypan blue, and 57 per cent of the unprotected animals were thus treated. These figures seem to indicate that the addition of the dye decreases the animal's chance of surviving by about one-half. Since it is clear that "clasmatocyte transfer" is as good in animals given dye as in those not receiving it, it appears that the dye in some way interferes with the functioning of the cells in the pleural cavity.

Since a more detailed study of the process of clearing up was desirable and since a preliminary experiment had shown that the critical period in the sterilization of these animals lay between forty-eight and seventy-two hours after infection, a number of rabbits were treated similarly to those in group 2 and killed at intervals of from twenty-four

TABLE 3.—*Summary of the Study of Exudates of the Right Pleural Cavities of Rabbits with a Peritoneal Focus of Clasmatocytes, Killed at Intervals After Infection in the Right Pleural Cavity with from 100 to 260 Times the Minimum Lethal Dose of Passage Fluid Streptococcus "H"*

	Number Organisms Given	Number Organisms Recovered per Cc.*	Amount of Fluid, Cc.	Total Cells*	Total Clasmatocytes	Total Polymorphonuclears	Percentage Clasmatocytes	Percentage Polymorphonuclears	Percentage with Streptococci: Clasmatocytes	Percentage with Streptococci: Polymorphonuclears	Trypan Blue Cells: Percentage	Trypan Blue Cells: Number
Normal.....	.....	...	0.1	0.35	0.3	0.05	85	15	..	..	..	..
Control† (3)...	.....	...	0.1	0.3	0.25	0.05	83	17	..	..	..	..
24 hour (7)....	3,400	127	5.2	359.0	17.0	342.0	8	92	0	3.7	0	0
48 hour (7)....	3,000	1.9	3.1	267.0	35.0	232.0	21	79	2	0	0	0
72 hour (8)....	3,000	Sterile	0.13	4.1	3.4	0.7	80	20	0	0	2	0.07
5099	4,400	Sterile	1.8	4.3	1.1	3.1	27	73	0	0	2	0.022

* In millions.
† Animals with peritoneal foci, killed without intrapleural infection.

to seventy-two hours. A less intensive study was made of animals between the three day and two week periods. A single animal was studied fifty days after the infection.

Table 3 shows the studies of the exudate of the infected cavities. In animals with a "peritoneal focus" that were killed without infection being produced, it was found that the presence of a large intraperitoneal focus of clasmatocytes did not have any effect on the pleural cavities either in regard to the amount of fluid contained in them, the number or kind of cells present or the character of the walls. In all these respects, they were normal at the time the streptococci were injected. These cavities contained 0.1 cc. of fluid, in which were found about 350,000 white cells. Of these, approximately 300,000, or 85 per cent, were clasmatocytes; the other 15 per cent were polymorphonuclears. Furthermore, clasmatocytes showing dye were not present in their walls or in their pleural exudates, and their subserous tissues were normal in thickness.

TWENTY-FOUR HOUR PERIOD

Between twenty-four and thirty-three hours after the administration of the test dose (from 100 to 250 times the minimum lethal dose), the character of the exudate had markedly changed. It averaged [42] 5.2 cc. of turbid fluid. The organisms had multiplied enormously, more than 40,000 times the number injected being recovered in the platings from the right cavity. The changes in the cells were no less marked. Both clasmatocytes and polymorphonuclears showed great, though unequal increases. Of the 359 million cells present, 342 million of them (92 per cent) were polymorphonuclears. The clasmatocytes, originally composing 85 per cent of the cells present, now were only 8 per cent of the total, although their absolute number was large (17 million). The proportion between the clasmatocytes and the polymorphonuclears was 1:20. Phagocytosis occurred only in polymorphonuclears and in only a small proportion of these cells (from 3 to 4 per cent). Organisms did not appear in the clasmatocytes, and cells with trypan blue were not to be found.

Thus, at this period an acute condition with enormous numbers of polymorphonuclear cells, extensive proliferation of the injected organisms and only a slight manifestation of any resistance on the part of the infected animal occurred.

Normal animals reacted to a fatal intrapleural dose of streptococci in twenty-four hours by the production of an exudate which is also composed of about 90 per cent polymorphonuclears. The total number of cells produced, however, was only about one fifth as great, and the number of clasmatocytes was one-third as high as in the animals with a "peritoneal focus" (Gay and Morrison [21]).

Histologically, the protected animals showed pleural walls with an acute inflammatory condition. Their width was increased, on the average, to 136 microns; it was due largely to an infiltration of polymorphonuclear cells and in small part to an increase in the number of monocytes. As was shown in the previous part of the work, the diaphragmatic surface under these conditions reacted to irritants more strongly than the parietal surface. At this period it was thickened to an average of 252 microns and was covered with a seropurulent exudate in which masses of bacteria were present. In both tissues the most striking feature was the amount of diapedesis of the polymorphonuclears, both from the capillaries and from the subserosa into the cavity. It is important to note that dyed cells were not to be found on the wall in any case, although the diaphragm showed a few. Fibrin was not present in the exudate or under the serosa.

The distribution of organisms was as follows: They were visible in large numbers in the seropurulent exudate along the wall and along the diaphragm, and in some places lay in tight masses against the serosal cells. None was found within these cells. In two of the animals a few free chains of streptococci were present below the serosa, the cells of which were swollen and drawn apart. Since a particular reaction did not surround these organisms, it is probable that their invasion had been a recent one.

The acute inflammatory condition of the exudate was thus reflected in the walls.

Twenty-four hours after the administration of the test dose, only relatively slight changes had occurred in the serosae of normal animals given a fatal dose.

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42. In the averages made at this period, the single animal which was found sterile (5099) is not included.

These changes were of the same kind, although far less marked, as those in animals with a "peritoneal focus"; namely, a polymorphonuclear infiltration, seropurulent exudate and swelling of the serosal cells.

A single animal (5099) was found sterile at this period (table 3). The possibility of a faulty inoculation in this case was ruled out by the cell counts. The number of cells in the cavity as well as the amount of fluid was relatively small, while the proportion of clasmatocytes (27 per cent) was much higher than in animals which had not become sterile. It is significant that in this animal alone, at this period, dyed cells appeared in the exudate, to the amount of 2 per cent of the clasmatocytes.

The histologic manifestations in this animal were as follows: the reaction was marked along the diaphragm and less so on the pleural wall. The polymorphonuclears in either situation were so few as to be negligible. The reaction was a mononuclear one and in the diaphragm consisted practically entirely of dyed clasmatocytes. This surface was 111 microns thick, while the wall averaged 80 microns. Dyed cells were not present in the latter situation. Organisms were not visible in either tissue. There seemed to be a striking correlation here between the clearing up of a streptococcic infection and the presence of clasmatocytes.

FORTY-EIGHT HOUR PERIOD

Forty-eight hours after the administration of the test dose (table 3), the average amount of fluid had dropped to 3.1 cc., and the number of organisms was about 1.9 million per cubic centimeter in contrast to the 127 million per cubic centimeter of the twenty-four hour period. In two of the animals killed at this period, the number of organisms was only about twice that injected. Of further significance is the fact that the clasmatocytes had doubled, while the polymorphonuclears were less than two-thirds as numerous as at the twenty-four hour period. Furthermore, the number of organisms was most reduced in animals which had the highest relative and absolute clasmatocyte counts. The average proportion between the two chief types of cells was now approximately 1 clasmatocyte to 6 polymorphonuclears. The only phagocytosis was confined to the clasmatocytes; polymorphonuclears were inert in this respect. Trypan blue cells were not found in any of the exudates in which they were sought.

The condition of the exudate at this period may be summed up by pointing out that there were increases in the number and proportion of clasmatocytes, with corresponding decreases in the polymorphonuclears and in the number of bacteria present. The average amount of fluid was also somewhat decreased. Phagocytosis by polymorphonuclears had ceased, and had begun in the clasmatocytes.

Normal animals given fatal intrapleural doses showed, after forty-eight hours, an increased amount of fluid over the twenty-four hour animals, about 12 cc. being present on the average. The cellular contents of this exudate was formed almost entirely of polymorphonuclears, the clasmatocytes amounting to less than 1 per cent of the total.

The histologic manifestations in the protected animals were interesting. The number of macrophages in the walls was greatly increased, and there was a corresponding diminution of polymorphonuclars, so that the average thickening of the wall remained about the same as at the twenty-four hour interval (115 microns). Large numbers of dyed clasmatocytes had entered the subserous tissues. Some of these contained cellular debris and polymorphonuclears. The streptococci were distributed as follows: most of them lay among the clasmatocytes in the

serous exudate above the intact serosa. They were also found within the serosal cells, and below them in the tissue, either free in the enlarged lymph spaces or within clasmatocytes. In some places, the serosal cells were swollen and drawn apart without giving rise to new cells to fill in the gaps thus formed. Hence, there was a portion of the wall left exposed and covered only by fibers of connective tissue. These places, however, had under them many fewer bacteria than were found under the swollen serosal cells. From this observation, it appears possible that the organisms entered the tissue by being taken up by the serosal cells, either actively or passively, and passed back by them into the subserosa where they were rephagocytosed by macrophages.[43] All stages in the digestion of cocci may easily be found in the subserous clasmatocytes at this period. The capillaries showed a monocytosis, but none of the monocytes in this position contained any trypan blue. A small number of clasmatocytes undergoing mitosis were present.

What has been said applies chiefly to the pleural wall. In the diaphragm, the acute condition of the twenty-four hour period persisted for a longer time. Here the polymorphonuclears were more numerous, and the serosa was broken and even stripped off in places. At this period in the single animal with an infected peritoneal cavity (5088), organisms could be found free throughout the diaphragm. Dyed cells were also scattered throughout but occurred chiefly at the pleural and peritoneal surfaces. Mitotic figures, particularly of serosal cells, were frequent.

The most striking histologic feature at this period is the simultaneous appearance of large numbers of clasmatocytes and of streptococci below the serosae of the infected areas.

Forty-eight hours after the administration of the test dose, the normal controls showed histologically an extension of the acute inflammation which was beginning at twenty-four hours. The serosa was necrotic and was covered with an irregular fibrinopurulent exudate. Mononuclear cells were not visible either above or below the serosa. The capillaries showed masses of polymorphonuclears but not any mononuclear cells. Numerous streptococci were scattered throughout the exudate, although there had not been any infiltration of organisms into the subserous tissues.

SEVENTY-TWO HOUR PERIOD

Seventy-two hours after the injection of organisms, five of the animals killed were found to have sterile right cavities. Of the other three, twenty organisms were found in one, and in the two others one colony was obtained on the 1:100 dilution plates. The amount of fluid present was below normal in all the animals except one. The total number of cells, while still considerably greater than normal, was greatly reduced in comparison with the number previously present. The change in cellular character was pronounced: 80 per cent of the 4 million cells were clasmatocytes, and the ratio between these cells and the polymorphonuclears had risen to 1:0.25. Phagocytosis was not found in the animals which were still infected, due, no doubt, to the small number of organisms remaining. In two of the animals, dyed cells had appeared in the cavities.

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43. Cunningham (Am. J. Physiol. **62**:253, 1922) showed that most particulate matter is removed from the peritoneum by being forced into the cytoplasm of the serosal cells through the movements of the diaphragm against the viscera; the amount carried into the subserosa by phagocytes is small.

At this period and up to death, which usually occurred after five days, normal animals showed only polymorphonuclears in their exudates, increasing numbers of which were undergoing disintegration. The amount of fluid increased steadily and some times amounted to 25 or 30 cc.

Histologically, these animals showed a deep deposit of fibrin above an entirely necrotic serosa. In the subserosa, necrotic changes were also apparent: polymorphonuclear cells and muscle bundles were undergoing a decided disintegration. Fibrin and plugs of streptococci had appeared in the subserous lymph spaces. More macrophages were present than on the previous days and seemed relatively unaffected by the general necrosis, but their number was small.

A decided contrast is furnished by the observations for the seventy-two hour "peritoneal focus" animals. The wall averaged 100 microns, which was slightly less than at the former periods. The tissue was rapidly returning to normal. The number of monocytes was somewhat reduced over the previous intervals, and a large proportion of them showed their clasmatocytic nature by the storage of trypan

TABLE 4.—*Cells in the Peritoneal and Left Pleural Cavities of Animals with a "Peritoneal Focus" Infected in the Right Pleural Cavity with 100 to 250 Times the Minimum Lethal Dose of Passage Fluid Streptococcus "H" and Killed at Intervals Thereafter*

	Peritoneum				Left Cavity				Heart's Blood: Number of Animals with	
	Percentage	Percentage	Number of Animals with		Percentage	Percentage	Number of Animals with			
Time, Hours	Clasmatocytes	Polymorphonuclears	Infected Cavities	Sterile Cavities	Clasmatocytes	Polymorphonuclears	Infected Cavities	Sterile Cavities	Infected Cavities	Sterile Cavities
0	64	36	...	...	95	5	...	...	...	...
24	83	17	1	5	17	83	7	1	3	3
48	93	7	1	6	12	88	5	2	2	5
72	70	30	0	6	92	8	0	8	0	8

blue in their cytoplasm. Most of the few polymorphonuclears present were within macrophages. The serosal cells were still swollen and in some places were two or three layers in thickness. Fibroblasts were more prominent than heretofore, and a few giant cells were to be found. Organisms did not occur in any of the walls.

The diaphragm seemed to return to normal even more rapidly than the wall. The serosa was intact and an excess of cells was not present below it, nor were any organisms visible. Polymorphonuclears were not present, and the clasmatocytes were of the small type usually found in normal connective tissue; the fibroblasts were more prominent numerically than in normal tissues.

The peritoneum and the left cavity may be more briefly considered. The conditions found in them are summarized in table 4, which gives the percentages of cells and also the number of animals having infected or sterile cavities at the various intervals.

In the peritoneum, the number of clasmatocytes rose steadily through the twenty-four and forty-eight hour periods, but at seventy-two hours it had returned nearly to the normal proportion. The amount of fluid was never increased, even when the organisms had invaded the cavity, as they had done in two instances. One seems justified in supposing that lack of any acute condition here, even when

infection had occurred, and the steady increase in the proportion of clasmatocytes were the result of the presence of large numbers of these cells in the subjacent tissues and in the omentum.

Microscopically, the peritoneal wall did not show any recognizable changes. The possibility of recognizing such differences is, of course, small, on account of the great area of the wall and the large number of cells present in it.

The course of events in the left cavity was essentially similar to that in the right. The clasmatocytes dropped sharply during the first twenty-four hours and declined slightly further at forty-eight hours. By seventy-two hours, however, they had returned to their normal proportion and the cavities were sterile. The average amounts of fluid paralleled this course of events exactly, increasing and falling with the percentage of polymorphonuclears. Thus the chief difference between the two cavities lay in the speed with which they reacted with a clasmatocytic exudate. As has already been pointed out, in the right cavity the

TABLE 5.—*Duration of Immunity. Study of Animals with a "Peritoneal Focus" That Have Recovered from Initial Infection and Have Been Reinoculated with Varying Doses of Passage Fluid Streptococcus "H" at Intervals Thereafter*

Rabbit	Trypan Blue	Streptococci in Immunizing Dose	Interval	Streptococci in First Test Dose	Result	Interval	Trypan Blue	Streptococci in Second Test Dose	Result
5032	0	2,150	20 days	2,100	Survived	30 days	0	7,250	Survived
5034	0	2,150	20 days	2,100	Survived	30 days	30 cc.	7,250	Survived
5038	0	2,150	30 days	1,200	Survived	30 days	0	2,500	Survived
5035	0	2,150	30 days	1,200*	Survived	30 days	30 cc.	2,500	Survived
5015	0	950†	30 days	1,550	Survived	20 days	30 cc.	2,750	Survived
5016	0	950	30 days	1,550*	Survived	20 days	0	2,750	Survived
5024	0	1,200	20 days	1,550	Survived	20 days	0	2,750	Survived
5025	5 cc.	1,200	20 days	1,550*	Survived	20 days	30 cc.	2,750	Survived

* Inoculation made in left pleural cavity.
† Normal control animal with this dose died in six days.

clasmatocytes reached their low point at twenty-four hours and thereafter increased rapidly in proportion. This difference may be due to the greater stimulus given the right cavity.

Sections of the left cavity taken at twenty-four hours showed a wall somewhat less than twice normal in thickness. Dyed cells were not present; there was a small polymorphonuclear infiltration and a noticeable increase in the monocytes. The diaphragm did not differ essentially from the wall except for the presence in it of dyed cells. At forty-eight hours the mononuclears were more prominent numerically, although the number of cells was always small in comparison with the right cavity. Dyed cells had appeared, and organisms when present were found in and below the serosal cells and undergoing digestion in the subserous mononuclears. At seventy-two hours, the tissue was practically normal: the subserous lymph spaces were enlarged and the serosal cells were slightly swollen. Dyed cells were rarely found, and the bacteria had disappeared.

Of the other organs studied, namely, the spleen, the mesenteric lymph nodes and the right and left superior retrosternal lymph nodes, all were found normal or else had suffered changes not recognizably different from those of the normal infected controls.

The study of animals killed at intervals beyond the three day period showed that the course of events previously indicated continued until an approximately normal condition had been recovered. Thus, the pleural walls and diaphragms of animals killed at five, seven and fourteen days showed tissues in which regressive changes were predominant. That this process is not invariable is demonstrated by the condition of the single animal killed at nine days. Here a chronic infectious condition had set in, and 7 cc. of fluid was present. The tissues surrounding the pleural cavity showed granulating areas of great thickness, that on the diaphragm being more than 1 mm. wide. The cavity had thus been treated much like an abscess and walled off from the rest of the body by granulation tissue. The outcome of an infection of this sort cannot, of course, be determined, although previous experience has shown that animals in which a chronic condition is set up usually recover. Symptoms of infection were not present in the animal when it was killed. A single animal was allowed to survive the infecting dose for fifty days. Histologically, the pleural cavities were normal except for the presence here and there in the subserosa of nests of mononuclears; the peritoneal wall, which showed decided evidence of regressive changes, was still about twice the normal in thickness and contained numerous clasmatocytes.

DURATION OF IMMUNITY

Several of the animals in which a peritoneal focus had been formed and which had survived the intrapleural streptococcic infection were tested for the duration of their immunity. Table 5 gives a summary of this phase of the work. Twenty or thirty days after the dose to test the efficiency of the peritoneal focus, the animals were reinjected intrapleurally with varying amounts of streptococci. In three of them, the reinoculation was in the left cavity. All the animals survived. While some of the doses given were comparatively small, they were still many times the minimum lethal dose (from 80 to 140 times).

After a further interval of twenty or thirty days (i.e., from forty to sixty days after the formation of the peritoneal focus), the animals were again injected with streptococci. This time, however, one of each pair of animals was given 10 cc. of a 1 per cent aqueous solution of trypan blue intraperitoneally each day for the three days preceding the second test dose; 30 cc. of the dye was thus injected. The dye was given to these animals in an effort to ascertain if their immunity could be negatived by a blocking of the clasmatocytes. As the table shows, both the rabbits that received the dye and those that did not were completely protected, even against approximately 450 times the minimum lethal dose.

One should recall here the fact already pointed out that even fifty days after the infection of a peritoneally treated animal a considerable focus of clasmatocyte still remains in its peritoneum. At the same period the pleural surfaces were normal, except for a few small nests of mononuclears. At fourteen days they were also near normal, while the peritoneal focus was still large. Hence, it is probable that at least for a considerable period after its formation the cells of the peritoneal focus

were available in either pleural cavity for the clearing up of infection by streptococci and might have been responsible for the immunity which was present. The failure of the trypan blue to destroy the immunity may have been due to a stimulating effect of the dye on the reticulo-endothelial system, rather than to the depressing effect expected. Thus, Goldzieher and Peck [44] recently showed that the response to infection of the reticulo-endothelial system in vitally stained animals, while less at first, eventually was greater than in unstained controls. The same was found to be true on the injection of toxins. In a recent review of this subject, Gay [45] pointed out that such results are by no means inconsistent with prevention of formation of antibodies or of immunity by dyes, since, as is well known, substances of this sort may have diametrically opposite effects on the body, depending on the amounts in which they are used.

COMMENT

Although the phrase "clasmatocyte transfer" has been used to indicate the process described in the present paper, an assumption has not been made, thereby, that the normal sources of tissue macrophages have failed to supply their usual quota to the irritated area. It must necessarily be true that these places of origin have been stimulated during the formation of the peritoneal focus, since such an enormous increase of clasmatocytes could hardly have come exclusively from cells scattered in the tissues, and since the usual sources have not been interfered with in any way. There are, however, several observations which tend to show that the focus itself is actually the source of many of the cells mobilized in the subsequently irritated area. Histologically, the spleen and mesenteric lymph nodes, from which are derived the monocyte group in general, do not show any more activity in their germinal centers or in their reticulum in animals with a "peritoneal focus" than in animals which merely have an intrapleural irritation. Secondly, in the experiments of Nakahara,[37] a change was not found in the blood picture on the formation of a peritoneal exudate of macrophages; in white cell counts made in this laboratory [46] during experimental transfers between the right and left pleural cavities, material differences could not be detected in the number or proportion of monocytes in the blood, nor could any dyed cells be found in the blood. If cells of the monocyte type were actually being formed in the usual centers for their production in the large numbers found in the exudates, it would seem probable that they would appear in the blood stream in increased numbers. Further-

44. Goldzieher, M. A., and Peck, S. M.: Experimental Studies on Reticulo-Endothelial System, Arch. Path. **3**:629 (April) 1927.

45. Gay, F. P.: Local or Tissue Immunity, Arch. Path. **1**:590 (April) 1926.

46. Unpublished experiments.

more, the appearance in the wall and throughout the diaphragm of large numbers of dyed cells, under the stimulus of a streptococcic infection, points in the same direction, since dyed cells have never been found in the spleen and only irregularly and in small numbers in the mesenteric lymph nodes.

However, when the stimulus is not so great, as in the case of intrapleural irritation by aleuronat-starch, about the same number of dyed cells appear in the pleural walls of animals with a focus as without. This result may be explained on the assumption that the enormous numbers of clasmatocytes in the peritoneum take up the dye to the exclusion of cells in other parts of the body, while in animals without such a focus,

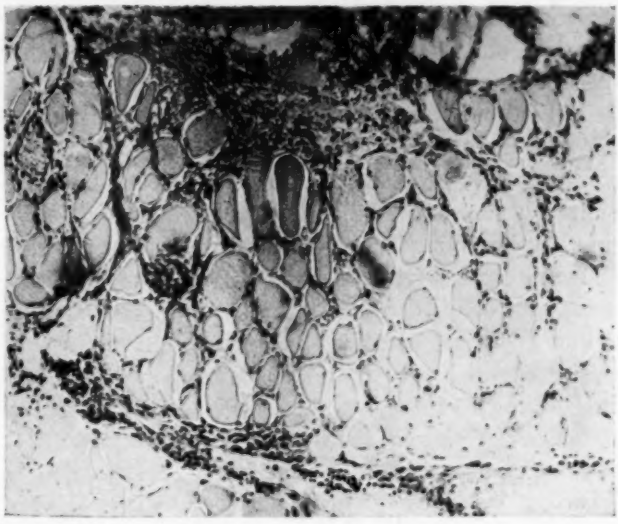

Fig. 2 (rabbit 5042).—Appearance of diaphragm of rabbit with peritoneal focus seventy-two hours after intrapleural streptococcic infection, showing the marked intramuscular invasion of clasmatocytes; × 120.

the dye is free to diffuse away to the rest of the body, including the pleural cavities, and stain the cells there present. Since the aleuronat-starch mixture is not a stimulus comparable to the streptococcus, the number of dyed cells drawn from the focus is only about equal to those stained by the dye in situ. Increased probability is given to this assumption by the observations in groups C and D (table 1). When a focus does not exist (group D), dyed cells are to be found in the pleural exudates and in the walls and diaphragm. When a focus is present, on the other hand (group C), its cells are loaded with dye, while none appears in cells of the pleural exudates and the subjacent tissues are free from it.

Following the vigorous stimulus of streptococci in the pleural cavity, numbers of dyed cells in process of migration may be discovered in the diaphragm (fig. 2). Furthermore, as has already been pointed out, in none of the monocytes in the capillaries has trypan blue ever been found. In this connection an interesting contrast is furnished by the average measurements during the first three days after infection of the peritoneal serosa of the diaphragm. That below the left cavity measures 48 microns, while the average for the portion adjacent to the right cavity is 90 microns; this thickening, as in similar thickenings in the pleurae, is due to the increased numbers of cells, many of which contain dye. Thus there appears a strong tendency for cells in the peritoneum to collect at the point nearest the irritation, preparatory, presumably, to their further migration through the diaphragm.

In this connection, it may be pointed out that the diaphragm is abundantly supplied with lymphatic channels. Küttner [47] stated that both the pleural and peritoneal surfaces are filled with lymph vessels, and MacCallum [48] has pictured the relationship between these lacunae and the mesothelial lining of the pleural and peritoneal cavities. Further, the network of lymph vessels of the peritoneal surface is closely connected with that of the pleural surface. As has already been shown these diaphragmatic lymph spaces become swollen during the pleural infection and in them may be found dye-filled clasmatocytes. Both Cunningham [49] and MacCallum [48] demonstrated that after the intraperitoneal injection of dyes, clasmatocytes loaded with the pigment may be found moving through the peritoneal serosa into the diaphragmatic lymph spaces.

Besides the lymph connections by way of the diaphragm, less direct channels between the two cavities have been demonstrated by various workers. Thus, Tenderloo [50] showed that the mediastinal nodes may be injected from those adjacent to the aorta in the peritoneum, and Franke [51] concluded that there is a direct union between these nodes and those of the lung. Beitzke [52] stated that there is a connection between the two cavities in the vessels which anastomose from the celiac glands to the diaphragmatic pleurae, and Küttner [47] demonstrated that the lymphatic glands of the liver also have a thoracic connection, especially to the left pleural cavity.

SUMMARY

In animals with areas of granulation tissue in the peritoneal wall, intrapleural irritation with aleuronat and starch mixture results in the

47. Küttner, H.: Beitr. z. klin. Chir. **40**:136, 1903.
48. MacCallum, W. G.: Bull. Johns Hopkins Hosp. **14**:105, 1903.
49. Cunningham, R. S.: Am. J. Physiol. **62**:248, 1922.
50. Tenderloo, N. P.: München. med. Wchnschr., 1904, p. 35.
51. Franke, C.: Zey, Beitr. Path., 1912, p. 54.
52. Beitzke, H.: Verhandl. d. deutsch. path. Gesellsch., 1908.

production of an exudate and of a subserous infiltration richer in clasmatocytes than in animals without such a peritoneal focus of cells.

When from 100 to 250 times the minimum lethal dose of a highly virulent strain of hemolytic streptococcus is used intrapleurally in place of the aleuronat and starch mixture, the animals are found to be protected in 73 per cent of the cases. The detailed study of the changes that occur under these circumstances in the pleural wall and pleural exudates strongly suggests that participation of clasmatocytes from the peritoneum is the basis for the intrapleural immunity produced.

Reinoculation of the cavities with multiples of the minimum lethal dose shows immunity in both pleural cavities for at least twenty days and in the right cavity for at least thirty days. The animals are also found immune to a second intrapleural inoculation given from forty to sixty days after the formation of the peritoneal focus.

THE SEDIMENTATION RATE OF ERYTHROCYTES

ITS RELATION TO FIBRIN VALUE AND CHOLESTEROL CONTENT AND ITS APPLICATION IN TUBERCULOSIS *

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Recently a clinical trial of sodium aurothiosulphate was undertaken at the Detroit Municipal Tuberculosis Sanatorium. The laboratory was called on to assist the clinical department with whatever procedures seemed promising to furnish reliable data in regard to prognostication and evaluation of progression or retrogression of the lesions and the general condition of the patients. Among other procedures, determinations of the erythrocyte sedimentation rate and of the plasma proteins were selected. The literature on these subjects, which has recently been reviewed by one of us,[1] indicated that the desired information might be gained by these procedures. On the other hand, it was expected that this work would afford an unusually good opportunity for appraising the values of the laboratory procedures as compared with the clinical observation. The latter—under the auspices of Drs. J. B. Amberson, Jr., and B. T. McMahon—was planned and executed with minute care, including frequent physical examinations and monthly roentgenograms for each patient. The laboratory workers did not have any knowledge of the clinical course, and the clinical workers did not receive the results of our prognostic tests during the actual work, so that the control of our methods was effected not only with the utmost care, but with complete impartiality at the same time. The first analysis of the results was so far from anything that the literature seemed to promise, that it was decided to elaborate and complete this part of the work. The investigation was limited to a few definite and essential points. Attention and further work was centered on the following problems: (1) the relation of the fibrin and cholesterol content of the blood to the sedimentation rate; (2) the fluctuations of the sedimentation rate in normal persons, again in relation to blood fibrin and cholesterol; (3) the clinical significance of the sedimentation rate and fibrin determinations in clinical tuberculosis.

METHODS

The lack of a uniform technic for the performance of the sedimentation test has frequently been commented on, and this has usually

* From the William H. Maybury Sanatorium (Detroit Municipal Tuberculosis Sanatorium).

1. Pinner, Max: Die Serodiagnose der Tuberkulose, Leipzig, J. A. Barth, 1927.

been followed in the same paper by the advocating of a new technic. The various technics, modifications and improvements now number well over twelve. As far as we can see, none of them meets the requirements of simplicity and reasonable correctness any better than the one suggested by Westergren,[2] nearly ten years ago. Many so-called micromethods have been suggested, none any simpler than the one described by Fåhraeus.[3] This author warned that micromethods may yield less accurate results.

In these studies, Westergren's method was used in one series of patients. In one group of patients in whom simultaneous studies of the blood chemistry were performed, Westergren's method was followed, but oxalated blood was substituted for citrated blood in order to allow the performance of all examinations on the same blood sample. The sedimentation rate of oxalated blood differed from that of citrated blood. A series of duplicate tests showed that low sedimentation rates are usually higher in oxalated blood than in citrated blood, and that with high rates the relation is frequently reversed. A definite numerical relation could not be established. In a third series of patients Cutler's [4] technic was followed, since this author made particularly promising statements in regard to this test. In the latter two series of patients, the rate of sedimentation was read at five minute intervals, but only the total drop after the first hour is recorded here.

The blood used for estimations of fibrin and cholesterol was drawn in the morning before the subject had breakfasted. Any effects of venous stasis on the composition of the blood (Plass and Rourke [5]) were minimized by making the time of constriction as short as possible. A sufficient amount of a 20 per cent solution of potassium oxalate was used to bring the concentration of oxalate to from 0.2 to 0.4 per cent; in some cases an equivalent amount of the dry salt was used.

The cholesterol content of whole blood was determined by the method of Myers and Wardell.[6] Small Soxhlet outfits were used for the extractions which were continued for one and one half hours to insure the complete extraction of cholesterol. The standards were chloroform solutions of cholesterol. Values obtained from duplicate extractions agreed with each other within less than 5 mg. per hundred cubic centimeters.

Fibrin values were determined according to Wu.[7] Duplicate determinations gave values differing by not more than 0.01 per cent.

2. Westergren: Ergebn. d. inn. Med. u. Kinderh. **26**:577, 1924; Am. Rev. Tuberc. **14**:94, 1926.

3. Fåhraeus: Acta med. Scandinav. **55**:1, 1921.

accurate results.

4. Cutler: Am. J. M. Sc. **171**:882, 1926.

5. Plass and Rourke: J. Lab. & Clin. Med. **12**:135, 1927.

6. Myers and Wardell: J. Biol. Chem. **36**:147, 1918.

7. Wu: J. Biol. Chem. **51**:33, 1922.

NORMAL VALUES

In establishing normal standards for the sedimentation rate or for data concerning the blood chemistry, one may follow either of two procedures. One may examine a series of normal persons under ideal, physiologic conditions, such as boys in college, and "ideally normal" values will be obtained. For clinical purposes, however, it may be more convenient to follow the dividing line which is of practical significance, i. e., the line between clinically healthy and clinically diseased persons. In this way, persons working under greater stress and afflicted with more of the unavoidable but unnoticed and unnoticeable ailments of a normal working life, who might be excluded from the "ideally normal," are included, and values are obtained which are probably more truly "practically normal." The latter selection was made for the present studies and may account for certain divergencies from previous authors. It must be emphasized that we were careful to exclude from our normal group any persons who had noticeable minor ailments.

The maximum sedimentation rates for the first hour are, according to Westergren, for males 3 mm., borderline normal 7 mm.; for females 7 mm., borderline normal 11 mm. Fåhraeus' figures for the average normal are 3.3 mm. and 7.4 mm., respectively; he considers any rates higher than 9 mm. for men, and 12 mm. for women, pathologic. Our average normal, when Westergren's technic is used, for both sexes, is 3.2 mm., maximum normal 7 mm. (calculated from thirteen tests on thirteen persons). We did not find any data in the literature regarding normal rates obtained with oxalated blood. Fourteen clinically normal persons were examined in thirty-seven tests with oxalated blood. The calculated average normal rate was 8 mm.; the maximum normal rate 16 mm. Most of the tests with oxalated blood were done simultaneously with, and with the same blood samples as, the tests with citrated blood. The additional tests represent repeated tests on the same persons. Since our values for citrated blood tally well with Westergren's figures, it must be assumed that our normal rates for oxalated blood are fairly correct. With Cutler's method we obtained decidedly higher normal rates than did Cutler and Greisheimer.[8] We examined clinically normal persons, being particularly careful to rule out those with any minor ailments, such as chronic sinusitis; our average normal was 12 mm., our maximum normal 23 mm. The latter value was obtained in an apparently healthy and husky mechanic, who for 18 months since the performance of the test has never shown any signs or symptoms of disease, under conditions of strenuous labor. Values obtained on normal women during menstruation, in the premenstrual and postmenstrual period, are not included in our normal values. The normal values for fibrin, according to the literature, vary between 0.1 and 0.35 Gm. per

8. Greisheimer: Am. J. M. Sc. **174**:338, 1927.

hundred cubic centimeters of plasma, depending on the method used (Süssmann [9]). Sweany, Weathers and McCluskey,[10] who used the same method as we did in our studies, calculated from four patients an average normal of 0.237 Gm., with a maximum of 0.282 Gm. and a minimum of 0.180 Gm. We made thirty-one determinations on eight persons, and obtained an average normal of 0.253 Gm., a maximum normal of 0.317 Gm. and a minimum normal of 0.156 Gm. The greater number of our determinations accounts for the much wider variations.

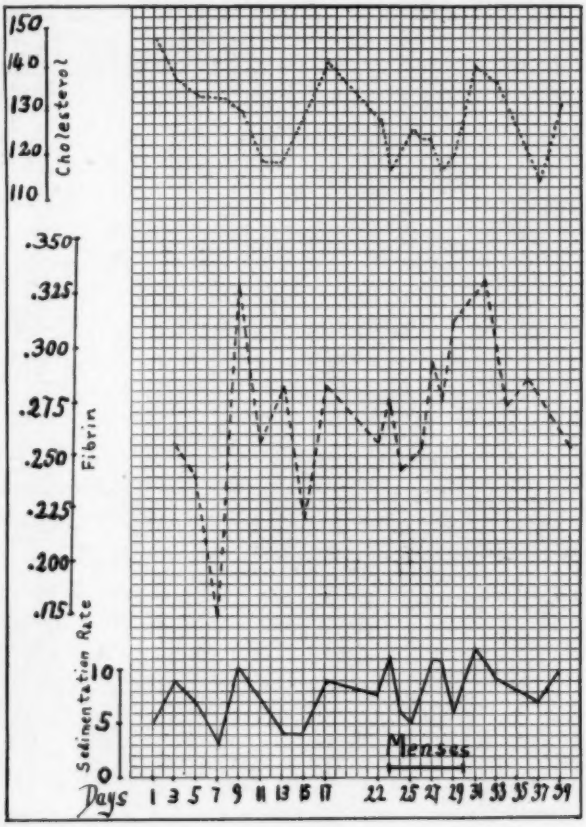

Chart 1.—Cholesterol, fibrin and sedimentation rate in a normal female. The dotted line indicates the cholesterol; the broken line, the fibrin, and the black line, the sedimentation rate.

THE ALLEGED CONSTANCY OF THE SEDIMENTATION REACTION

The relatively small variations in the sedimentation rate which are accepted as within normal limits presuppose that the reaction is practically constant in normal persons. Grafe and Reinwein [11] claimed that

9. Süssmann: Arch. f. Kinderh. **76**:182, 1925.
10. Sweany, Weathers and McCluskey: Am. Rev. Tuberc. **8**:405, 1924.
11. Grafe and Reinwein: Beitr. z. Klin. d. Tuberk. **54**:402, 1923.

an elevation of the rate of at least 3 mm., following an injection of tuberculin, is proof for the existence of an active tuberculous focus. Since far greater fluctuations occur spontaneously in normal persons, it is evident that these claims are unjustified. Chart 1 shows the fluctuations in one perfectly normal person. Probably more important, even, is the fact demonstrated in chart 2 that quite minor ailments, which in no way incapacitate or even seriously inconvenience the per-

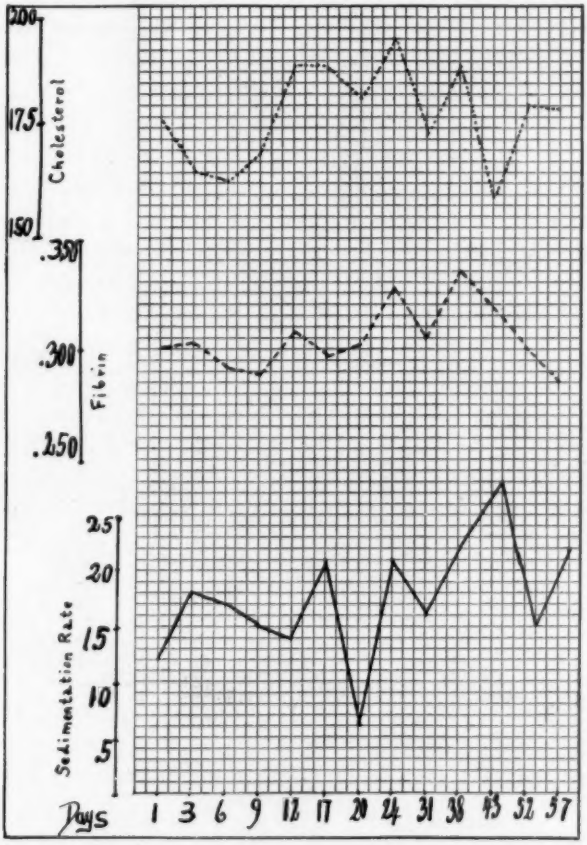

Chart 2.—Cholesterol, fibrin and sedimentation rate in a man with minor ailments which neither incapacitated nor seriously inconvenienced him. The dotted line indicates the cholesterol; the broken line, the fibrin, and the black line, the sedimentation rate.

son in question, cause marked variations. Chart 2 represents data of a man with bilateral apical fibrosis which was inactive as to signs and symptoms; he had, further, a chronic pansinusitis which did not cause any symptoms during the period of observation. Essentially similar curves were obtained on other normal persons and on persons with

slight chronic impairments. Fluctuations of the same magnitude have frequently been considered as diagnostically and prognostically significant in tuberculosis.

ALLEGED RELATION OF THE SEDIMENTATION REACTION TO THE FIBRIN CONTENT

Starlinger [12] and Frisch and Starlinger [13] state definitely that the sedimentation rate is strictly dependent on the fibrin content of the plasma. Starlinger's evidence is a table wherein the observations on twenty patients are enumerated; the fibrin content, determined by refractometry, increased in fair regularity with increasing sedimentation rates. It is not evident from his paper whether this table contains all his data or that from a selected group of patients; the latter possibility is suggested by the fact that the protocol numbers, starting with 1, go as high as 100. The same author presents additional evidence purporting to show that when some of the fibrinogen is absorbed by kaolin, bolus alba and animal charcoal, the sedimentation rate decreases. These latter experiments cannot be accepted as arguments for the author's claim, since the absorbents mentioned absorb other substances besides fibrinogen and bring about decided changes in the electric potential of the plasma. Popper and Kreindler [14] claim that an "indiscutable rélation" exists between the sedimentation rate and fibrinogen, "sans pouvoir toute fois affirmer l'existence d'un parallélisme absolu." It requires an unusual amount of optimism to consider this "indiscutable rélation" proved by their data, which are as follows:

Sedimentation Rate	*Fibrinogen*
4	0.218 ←
5	0.104 ←
7	0.432
8	0.222
8	0.432
15	0.436 ←
15	0.654 ←
18	0.432
18	0.868
19	0.432
19	0.322
20	0.432
22	0.751
22	0.761 ←
22	0.216 ←
22	0.652
24	0.436

12. Starlinger: Biochem. Ztschr. **114**:129, 1921.
13. Frisch and Starlinger: Med. Klin. **17**:1147, 1921.
14. Popper and Kreindler: Ann. de méd. **17**:57, 1925.

In chart 3 are assembled our data concerning the relation of the sedimentation rate to fibrin content. Both determinations were always made on the same sample of blood. For each sedimentation value the corresponding fibrin value is indicated by a dot. Two hundred and eighteen sets of tests are charted. One glance at the chart suffices to

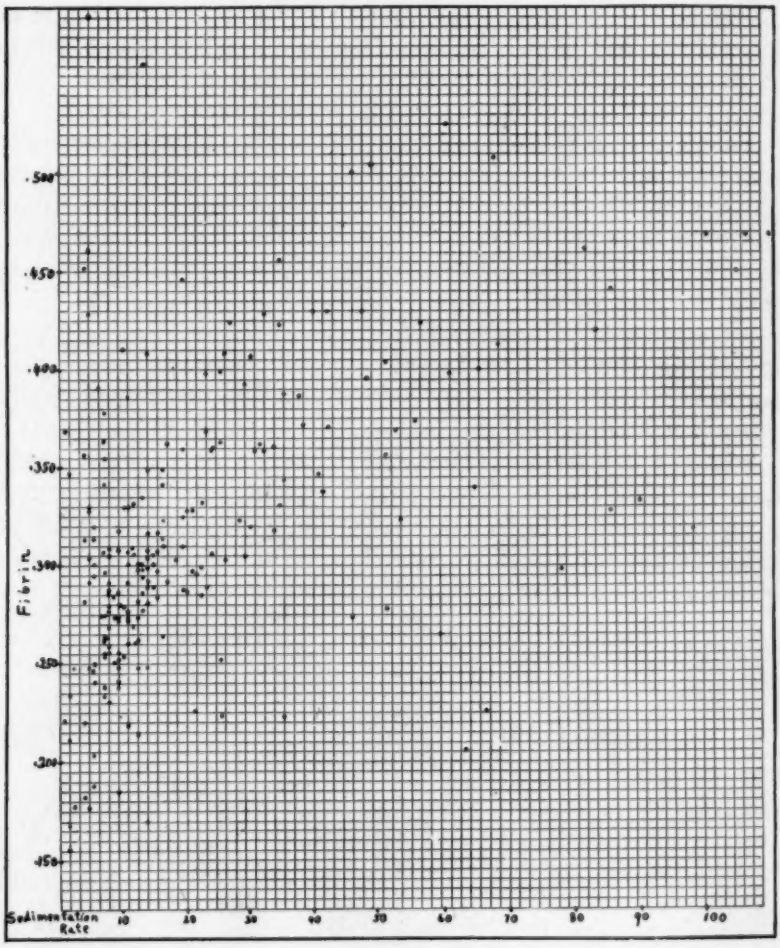

Chart 3.—Corresponding fibrin values and sedimentation rates; results from 218 blood samples.

demonstrate that under the given condition a lawful relation between the two sets of data does not exist. The only possible relation may be the fact that high sedimentation rates did not occur in the presence of low fibrin values; the number of high rates, 50 or more, is too small to warrant stressing this point.

The question arises whether the alleged relation between sedimentation and fibrin value may exist within one and the same patient. Chart 1 shows that this is not the case in normal persons; chart 2 demonstrates the same fact for conditions of slight disturbances, and chart 4 assembles

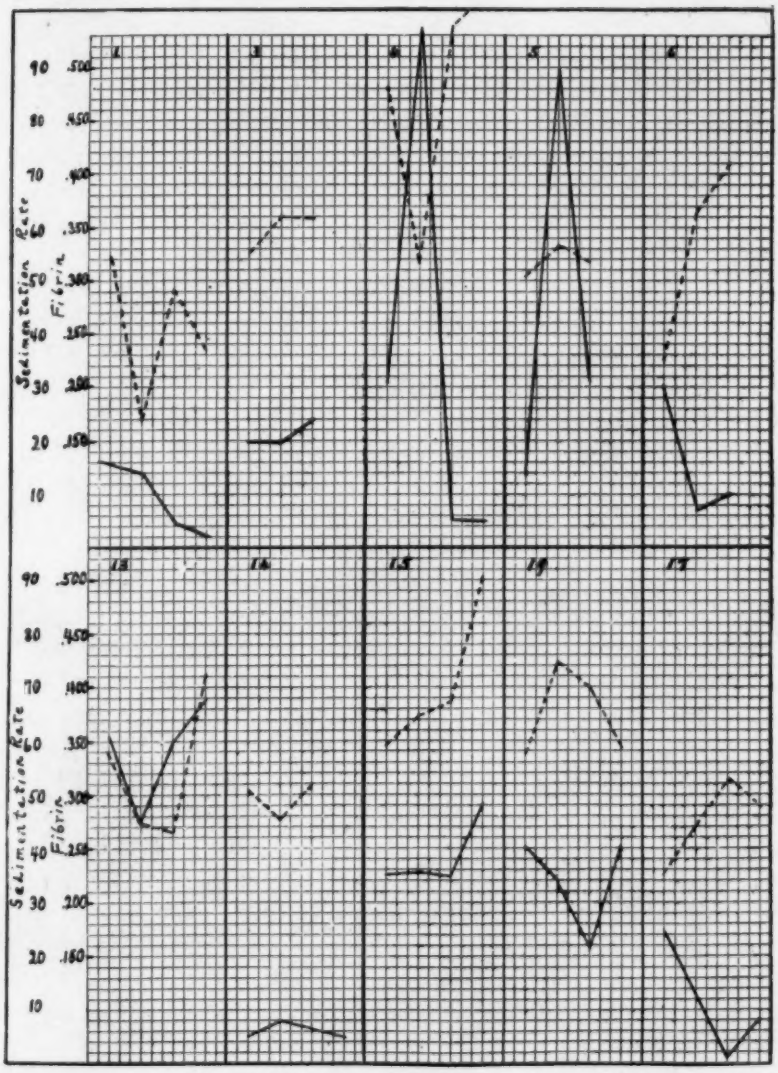

Chart 4.—Fibrin and sedimentation rate in patients with active tuberculosis. Broken line indicates fibrin; black line, sedimentation rate.

the analogous data on ten patients with active pulmonary tuberculosis. Chart 4 shows that a lawful relation does not exist. Materially the same results were obtained in thirty other tuberculous patients. In

forty tuberculous patients the fibrin content and sedimentation rate were determined at intervals of from four to ten weeks; in this way the simultaneous fluctuation could be compared in seventy-five sets of values; in only thirty-one of these did the fluctuations occur in the same direction, while forty-four did not fulfil the theoretical expectation.

ALLEGED RELATION BETWEEN SEDIMENTATION RATE AND CHOLESTEROL CONTENT

Kürten [15] showed that the addition of cholesterol to blood increased the sedimentation rate, and that lecithin had the opposite effect. Grossmann [16] and Lasch [17] emphasized the accelerating action of cholesterol; the former showed that this action was independent of alterations in the proteins. He produced alimentary hypercholesteremia in rabbits and found that they had high sedimentation rates. Lasch emphasized the fact that high sedimentation rates were found in all diseases in which the blood cholesterol value was high, and that rabbits, made hypercholesteremic by poisoning with saponin, had blood cells of which the sedimentation rate was fast.

We tried to ascertain how regularly this alleged relation exists in human beings. Chart 1 shows the respective curves for a normal person, and chart 2 shows the same for a clinically healthy, although not quite normal, person. In chart 5 are plotted the cholesterol values in 140 simultaneous sedimentation tests on twenty-nine persons. In eighteen patients with active tuberculous pulmonary lesions the sedimentation rate and the blood cholesterol value were determined twice at an interval of from four to five weeks. In only ten cases did the fluctuations behave according to the statements of Kürten and Lasch.

THE CLINICAL SIGNIFICANCE OF THE SEDIMENTATION REACTION IN TUBERCULOSIS

Instead of a review of the extensive literature on this question, it will, no doubt, suffice to mention Westergren's opinion on the question. His standpoint is probably most widely accepted today, although dissenting voices are not entirely lacking. Westergren considers the sedimentation reaction "a valuable aid for the evaluation of the malignancy of a pulmonary tuberculosis at the time of examination." He believes that the rate runs closely parallel to the extent of the lesion, the amount of tissue destruction and the "activity" of the process. In this regard it is held to be a finer indicator than the temperature. Since the sedimentation is more accelerated in exudative processes than in

15. Kürten: Arch. f. d. ges. Physiol. **185**:248, 1920.
16. Grossmann: Ztschr. f. d. ges. exper. Med. **42**:496, 1925.
17. Lasch: Ztschr. f. d. ges. exper. Med. **42**:548, 1925.

productive processes, the test affords, according to Westergren, a certain prognostic indication, and this significance can be enhanced by repeated tests. The influence of chronic mixed infection is not known. Westergren considers it "at least highly improbable" that normal sedimentation rates are obtained in active tuberculosis.

Cutler—to quote a more recent American author—says, "The blood sedimentation test is a more reliable index of the presence or absence of activity than the temperature, pulse rate, gain in weight or physical

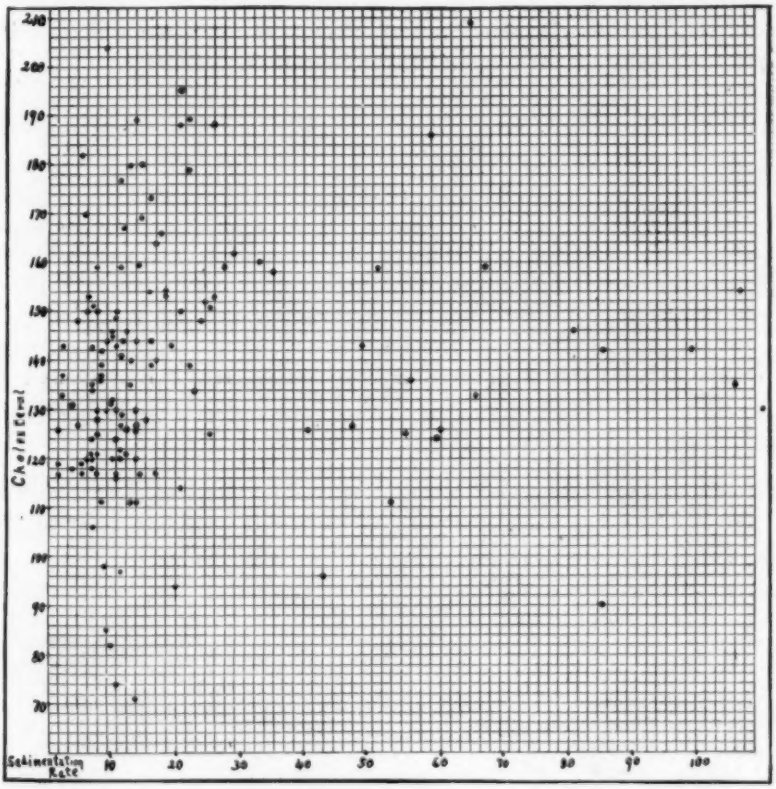

Chart 5.—Corresponding cholesterol and sedimentation rates; results from 140 blood samples.

signs." From the fact that he did not find a definite relation between the test and the extent of involvement, curved nails, clubbed fingers, duration of disease, duration of activity, bacillary content of sputum, expectoration and subjective condition, the conclusion is drawn "that in estimating activity the blood sedimentation test is more trustworthy than any one of the symptoms and signs enumerated."

We have used essentially two criteria to arrive at an evaluation of the clinical significance of the sedimentation test; namely, the percentage of

patients with definite active tuberculosis who have a normal rate, and the fluctuations of the rate in one patient compared with the clinical course of the disease. Table 1 shows by percentage the occurrence of normal rates in active tuberculosis.

Of the groups of forty-two patients, in whom sedimentation tests were performed with oxalated blood, five had values below the maximum normal on all examinations, performed from four to seven times. It has been reported frequently that during the terminal stage of tuberculosis both the sedimentation rate and plasma proteins may decrease to normal or subnormal values. Only one of our patients was examined shortly before death; she had a high sedimentation rate.

TABLE 1.—*Percentage of Normal Sedimentation Rates in Patients with Active Tuberculosis*

	Westergren's Method	Oxalated Blood	Cutler's Method
		Normal Average, 8 mm.	Normal Average, 12 mm.
	Highest Normal, 7 mm.	Maximum Normal, 16 mm.	Maximum Normal, 23 mm.
Number of tests	71	179	391
Number of patients	49	42	391
Number of tests below normal average	17 (23.9%)	60 (33.5%)	44 (13.8%)
Number of tests below maximum normal	..	88 (49.1%)	103 (26.3%)

TABLE 2.—*Correlation of Sedimentation Rate and Clinical Course*

	Patient's Condition Remained Stationary	Patient Improved	Patient Became Worse
Sedimentation rate remained the same (± 3 mm.)	1	5	2
Sedimentation rate decreased 3 mm. or more	4	5	9
Sedimentation rate increased 3 mm. or more	4	6	4

In forty of the forty-two patients, the clinical records were compared with the sedimentation reaction. In table 2 the data are briefly assembled.

It is evident, then, that a considerable percentage of patients with active disease and bacilliferous sputum have a rate within normal limits. The differential diagnostic value of a normal rate is, therefore, insignificant. The lack of correlation between the sedimentation rate and the clinical course is clearly shown in table 2. In this table the values only at the beginning and the end of the observation period are recorded. In twenty-two of the patients as many as three additional determinations were obtained between the recorded values. In analyzing these data, the lack of parallelism between the sedimentation rate and the clinical course becomes still more evident than from the brief statistical representation.

Only one conclusion apparently is possible, namely, that the sedimentation test is diagnostically and prognostically almost without value in clinical tuberculosis. What remains of the practical importance of this reaction is that a person in whom the sedimentation rate remains well above the normal limit on repeated examinations harbors some disease, and if the diagnosis of tuberculosis has been established in such a patient, with the exclusion of other pathologic conditions, by other means, the lesion can safely be considered active.

CLINICAL SIGNIFICANCE OF FIBRIN DETERMINATION IN TUBERCULOSIS

It has been claimed repeatedly that toxemia and the destruction of tissue alter the structure of the plasma proteins in such a way as to decrease their colloid stability. This is supposed to be brought about by a shifting of the proteins toward the more coarsely dispersed fractions, notably fibrinogen. That the amount of the latter gives a reliable numerical indication of the extent and progressiveness of tuberculous lesions has been claimed particularly by Frisch.[18] The studies reported here afforded ample opportunity to test these claims. Of 118 fibrin determinations in forty-two patients with active tuberculosis, ten, or 8.4 per cent, were below the normal average (0.253) and forty, or 33.9 per cent, were below the maximum normal (0.317). A comparison of fibrin fluctuations with the clinical course was made in eighteen cases, with two determinations for each patient, at an interval of from four to five weeks, and in twenty-two cases, with three or four determinations for each patient, over an entire period of seven months. Nine of the forty patients did not show any noticeable change in their clinical picture: in five of them the fibrin content decreased, and in four it increased. Sixteen patients improved: ten had an increase in fibrin value. Fifteen patients became worse, but only five of them showed an increase of fibrin content.

In the data presented a relation between fibrin content and clinical course cannot be detected. In a similar way, as in the sedimentation reaction, one finds a tendency—irregular, and quantitatively most deceptive—toward high values in active disease.

COMMENT

On a carefully controlled and quantitatively sufficient material, it was shown that several of the main statements of other workers concerning the sedimentation of erythrocytes could not be substantiated on the material presented. To recapitulate briefly, the important points were: 1. The normal variations are so wide as to lead to a considerable

18. Frisch: Beitr. z. Klin. d. Tuberk. **60**:141, 1924.

amount of overlapping of normal values—or at least of values obtained on perfectly normal persons—with values frequently obtained in active tuberculosis. Even when the normal values are kept close to the "ideally normal," a definite percentage of patients with active tuberculosis is found within these limits. 2. Neither the fluctuations of the sedimentation rate nor those of the fibrin content of the plasma afford a reliable indication of the clinical course of tuberculosis. 3. A quantitative relation does not exist between fibrin content and speed of sedimentation, nor between cholesterol content and sedimentation.

The apparent disagreement with the majority of previous workers on the same subject calls for some explanation. First, the normal standards accepted here are somewhat higher than the ones usually accepted. Some of the reasons for this have been discussed. Another reason may be found in the fact that all our determinations were performed on samples of blood taken before breakfast, i. e., after a period of at least twelve hours during which fluid was not taken. It may be expected that under such conditions the proteins of the blood are maximally concentrated (relative loss of water) yielding relatively high values for both fibrin and sedimentation. The fixing of standards, however, is only of relative importance; it is obvious that with low normal rates, a relatively large percentage of determinations on normal persons would fall within the range of data of pathologic significance; and with the acceptance of higher normal values, many data from pathologic conditions fall within the normal range. High standards increase the specificity of the test, with loss of sensitiveness; low standards increase the sensitiveness, with loss of specificity. Most of the normal standards in the literature have been established by computing a number of single determinations on a series of persons. The importance of conducting serial examinations on one person is clearly shown in the first two charts.

The two chief claims in regard to the clinical significance of the sedimentation test are that the rate is practically always increased in active tuberculosis and that the amount of this increase affords a fair estimate of the extent and progression of the lesions. The value of the former function is reduced to a negligible degree by the amount of overlapping between normal and pathologic data, as shown in table 1. The three series of tests presented in this table demonstrate a striking difference in the percentage of failures. This difference must not be taken as evidence for the superiority of one method. The true explanation of the difference is as follows: The majority of tests in which Cutler's method was used were performed on patients in whom the disease was far advanced, on, or shortly after, their entrance to the sanatorium. The forty-two patients mentioned in the second column of table 1 had, at the time of the tests, been in the sanatorium for a

considerable time and had been in bed for long periods. We have had the experience commonly, that when tuberculous patients underwent a period of rest after a more active form of life the sedimentation rate was reduced; this reduction took place regardless of physical improvement; in a similar way, increase of body weight might occur under the same condition, although the lesion progressed.

The patients in the first column of table 1 represent a rather mixed group in which the cases were incipient and far advanced.

As to the parallelism between sedimentation rate and the clinical course, one must remember that this statement is based chiefly on rather loose statistical methods. One hundred patients whose condition is far advanced and active have always a higher average rate than 100 whose condition is incipient and only slightly active. Statistics of this type, with variations in the method of classification, form the foundation for the foregoing assumption. If our patients are classified similarly, a neat and regular increase of the average sedimentation rate in parallelism with the extension of the lesions becomes evident. It cannot be emphasized too strongly that such procedure is as misleading as would be the attempt to predict the date of death of a given person by the use of the tables on life expectancy—the reliability of which will not be disputed, in the face of the prosperity of life insurance companies. The results of serial examinations on single patients, as shown previously, dispel all illusion of an alleged parallelism.

Several authors have emphasized that not only the hourly sedimentation rate, but especially the shape of the curves, obtained by plotting the progress of the process at short intervals, indicate the degree of activity. Based on this assumption, blanks have been put on the market on which a ready-made diagnosis as to activity is printed for every obtainable shape of curve. The latter is, of course, primarily dependent on the amount of sedimentation within one hour, barring rather irrelevant deviations. But it is evident that a horizontal curve (diagnosis: "normal or absolute quiescence") cannot be obtained in the presence of a high rate, and inversely, a diagonal curve (diagnosis: "slightly to moderately active") is impossible with a low rate. It is objectionable to offer to the practicing physician an unreliable method for the responsible diagnosis of "activity" in tuberculosis, endorsed, as it were, by the semblance of finality in printed blanks. The same author states that "by repeating the test at regular intervals, the true course of the disease can be graphically represented, for as the individual improves the graph should approach more and more the horizontal line." It "should" if the theoretical conclusions were correct, but practical application, as recorded here, shows that it does not. In the paper quoted attempts at verification of the mentioned desideratum are not reported.

In emphasizing the pronounced shortcomings of the sedimentation test in clinical tuberculosis, we do not wish to leave the impression that the sedimentation rate, is not related to toxemia and tissue destruction. The failure of its application appears, in fact, to be due partly, to its too great sensitiveness, which accounts for the inconveniently broad phase where normal and pathologic data overlap. Practical medicine, at present, is not interested in the diagnosis of what may be termed "subclinical conditions;" these undoubtedly are frequently manifested in a rise of the sedimentation rate. It remains true that most normal persons have most of the time a relatively low rate, and that tuberculous patients have frequently a high rate, but this is just about as much as can be said safely in regard to clinical application. We agree fully with one point that has been emphasized repeatedly, that a high rate—well above a maximum normal—indicates disease and warrants careful examination in the absence of diagnostic signs and symptoms. In considering the immense literature on the sedimentation test, it apparently is important to reduce this procedure to its proper place. The enthusiasm over it—undoubtedly enhanced by the ease of its performance—endangers not only its correct evaluation but the evaluation of therapeutic procedures as well. The test has been used frequently to control treatment: a reduction of the rate is invariably hailed as a convincing proof for the success of a therapy. Such has been the case in treatment with tuberculin, sodium aurothiosulphate, pneumothorax and thoracoplasty. It has even been suggested that the sedimentation rate be entered in the patient's record at the time of entrance to an institution and at the time of discharge, as a witness for the therapeutic accomplishment. It has been claimed that a normal rate in an apparently cured tuberculous patient proves that he is now a normal risk for life insurance, regardless of his history of tuberculosis. In all these applications it should not be forgotten that the rate decreases frequently on enforced rest, regardless of clinical progress. In reviewing our whole experience with the sedimentation test, we are forced to the admission that in every case of disagreement between the sedimentation rate and clinical judgment—barring only extremely high rates—the clinician was more nearly correct than the customary interpretation of the sedimentation reaction. Several previous authors have arrived at a more or less skeptical attitude regarding this point, but it appears that in no previous publication known to us was the clinical value of the sedimentation test denied to an equal degree.

This whole discussion intentionally does not include the application of the procedure in other conditions than tuberculosis, such as pregnancy or disease necessitating an operation. We do not have any data relative to them. The material concerning tuberculosis might, however, suggest the necessity of some more critical studies in other fields.

In the clinical application of a laboratory procedure, which always contains a definite subjective factor, disagreement may easily arise. It is much more astonishing that dissension should exist in regard to the comparison and alleged relation of definite sets of quantitative data, rate of sedimentation, fibrin and cholesterol. Granted the inadequacy and inaccuracy of all methods of fibrin determination, refractometric, nephelometric and colorimetric (a discussion of this subject is contained in the article by Süssmann), they cannot possibly account for some of the disagreements recorded here. Again the importance of serial examinations and of conducting a large number of examinations must be emphasized. It would be easy to pick out from our charts 3 and 5 a series of cases which would represent an ideal quantitative relation, but this would be misleading.

Fåhraeus' experimental studies established the fact that the formation of large aggregate of red cells is responsible for fast sedimentation. This phenomenon is almost exclusively dependent on the nature of the plasma, an opinion well substantiated by later experimental work (Höber and Mond,[19] Linzenmeier,[20] Starlinger, Kürten). Fåhraeus found that erythrocytes settle faster in plasma than in serum. Further studies led him to the conclusion that albumin has only a slight enhancing influence on the sedimentation, whereas globulin, and fibrinogen to a greater degree, exert a marked influence on the sedimentation. But neither fibrinogen nor globulin, in his study, showed a strict quantitative relation to the speed of sedimentation. Starlinger, then, stated the absolute correlation, and others followed (Duzár and Rusznyák,[21] Murahami and Yamaguchi [22]). All these studies show that there cannot be any doubt that an increase in fibrinogen causes an increase of the rate of sedimentation, provided everything else is equal. In the application of the tests to nonexperimental conditions, this most important qualification "everything else being equal" has been too much overlooked, and, what is more important, is hardly ever realized. This point apparently explains the entire question. Essentially the same reasoning applies to the statement that an increase of cholesterol accelerates the speed of sedimentation. It is well known that a number of factors and conditions influence the sedimentation rate in one way or the other, such as p_H, the relative amount of the protein fractions, cholesterol, lecithin, number of red cells, amount of hemoglobin, cyanosis, surface tension, inorganic substances, dialyzable protein cleavage products, potential difference between plasma and red cells and

19. Höber and Mond: Klin. Wchnschr. **1**:2412, 1922.

20. Linzenmeier: Arch. f. Gynäk. **113**:608, 1920.

21. Duzár, J., and Rusznyák, S.: Monatschr. f. Kinderh. **28**:25, 1924; abstr., Am. J. Dis. Child **28**:441 (Oct.) 1924.

22. Murahami and Yamaguchi: Ann. de méd. **15**:4, 1924.

intake of certain drugs. It is hardly conceivable that a phenomenon which is dependent on so many different, partly antagonistically, partly synergistically, acting factors of largely unknown interdependence, could, under natural conditions, show a strict quantitative relation with one or two factors exclusively. That this is the case neither for fibrin nor for cholesterol is evident from the material presented. The foregoing statement that the sedimentation rate is not quantitatively related to fibrin value or to cholesterol content, should, then, be modified to the statement that whatever quantitative relation may exist does not become evident under nonexperimental conditions.

Many papers have been published in recent years on the shifting of the proteins toward the coarsely dispersed, more easily precipitated fractions under conditions of toxemia and tissue waste. A number of plasma and serum reactions, diagnostic for such conditions, have been advocated, all based on the demonstration of a destabilization of plasma or serum (Frisch and Starlinger, Daranyi,[23] Matéfy,[24] Sachs and Klopstock,[25] Mündel,[26] Lange and Heuer,[27] Vernes,[28] Wegierko,[29] Montank,[30] Gerlóczy [31] and others). In all these reactions some protein precipitating agent is used. It is claimed that these reactions are standardized in such a way that the normal protein structure in plasma or serum is not disturbed, that, however, pathologically unstable plasmas or serums are more or less precipitated by them. The most interesting point in this work appears to be the fact that the results of these various reagents are widely different when used on the same serums. This indicates probably that Oettingen's [32] statement is correct that the plasma proteins, under pathologic conditions, undergo not only quantitative, but more important qualitative changes. This may be the reason for the fact demonstrated here, that a mere quantitative determination of fibrin content does not yield results comparable to the clinical course. It shows at the same time the problematic nature of all the empiric tests devised to demonstrate a shifting of the proteins toward the globulin and the fibrin. The literature does not seem to contain any definite data on qualitative alterations of plasma proteins under conditions of disease. Further studies may show whether the alleged qualitative changes are specific for individual diseases. As far as the present

23. Daranyi: Deutsche med. Wchnschr. **48**:553, 1922.
24. Matéfy: Med. Klin. **19**:725, 1923.
25. Sachs and Klopstock: Deutsche med. Wchnschr. **49**:1292, 1923.
26. Mündel: Klin. Wchnschr. **3**:1912, 1924.
27. Lange and Heuer: Deutsche med. Wchnschr. **50**:35, 1924.
28. Vernes: Compt. rend. Soc. de biol. **93**:5, 1925.
29. Wegierko: Wien. klin. Wchnschr. **38**:932, 1925.
30. Montank: Proc. Soc. Exper. Biol. & Med. **21**:547, 1923-1924.
31. Gerlóczy: Klin. Wchnschr. **1**:2134, 1922.
32. Oettingen: Biochem. Ztschr. **118**:67, 1918.

knowledge is concerned, the statement apparently is justified, that, not infrequently, high fibrin values are found in patients with active tuberculosis, but that this occurrence is not by far regular enough to be of diagnostic aid, and that the increase does not parallel the progression and the extent of the lesions to a degree sufficient for one to ascribe to fibrin determination any prognostic significance. The relative amount of the various protein fractions of the serum has been studied more frequently than that of the plasma. In this field there is much disagreement. Some authors, notably Alder,[33] claim a correlated increase of globulin with progressive disease; others are represented by Brieger [34] who states that "the only regularity of the serum protein curve in the healthy and still more so in the tuberculous, is its irregularity." We believe that fibrinogen and sedimentation rate may well be included in this statement.

SUMMARY

1. The blood of persons in perfect health not infrequently had a sedimentation rate markedly higher than the usually accepted normal values. The fluctuations of the rate in normal persons were found to be much greater than they are usually reported to be.

2. A quantitative relation between the fibrin content of the blood and the sedimentation rate could not be ascertained in clinical tuberculosis, under normal conditions or during slight physical disturbances.

3. The same was true for the alleged relation between cholesterol content and sedimentation rate.

4. Although a higher average rate is found in active tuberculosis than under normal conditions, this increase is far from constant and it is not parallel with the extent and the progressiveness of the lesions. The prognostic value of the sedimentation test is minimal, and with the exception of extremely rare instances, this test is not apt to furnish information beyond that gained by clinical and bacteriologic observations. The clinical value of fibrin determinations in clinical tuberculosis is of the same order.

5. The possible reasons for the disagreement between these conclusions and those of enthusiastic advocates of the test are discussed.

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33. Alder: Ztschr. f. Tuberk. **31**:10, 1919.
34. Brieger: Klin. Wchnschr. **2**:1162, 1923.

Laboratory Methods and Technical Notes

THE GRAM STAIN

I. A Quick Method for Staining Gram-Positive Organisms in the Tissues *

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Since Christian Gram,[1] in 1884, introduced the method which bears his name, it has been modified in many and various ways, which were principally applicable to smears. The violet used has been gentian violet, various methyl violets and crystal violet. These have been used without mordant and with aniline, aniline sulphate, phenol, formaldehyde, ammonium oxalate, sodium carbonate and, doubtless, others.

The iodine solution has usually been that containing one part of iodine, two parts of potassium iodide and three hundred parts of water. However, this too has been modified by the addition or substitution of alkalis.

For differentiation, alcohol of varying strength, methyl alcohol, aniline oil, acetone, acetone and alcohol, acid alcohol and other reagents have been used.

In addition, the counterstains have been equally varied.

Gram originally devised his method for the demonstration of organisms in the tissues. This it did satisfactorily, but the tissues themselves were poorly shown. For this purpose Weigert's [2] method for fibrin and gram-positive bacteria was found more satisfactory, and is, in various modifications, still in use for the demonstration of both fibrin and gram-positive organisms in the tissues. Several criticisms of the results obtained by this method may be brought forward. 1. It is time consuming, taking from ten or fifteen minutes to an hour and a half. This factor alone is a bar to its regular use on routine material. 2. It is often extremely difficult to remove the violet stain from the cell nuclei with aniline or aniline and xylene. In fact, many workers expect the nuclei to remain violet, and some authors recommend the use of hematoxylin as a nuclear stain,[3] apparently realizing the hopelessness of removing the violet from the tissue elements. 3. In the presence of violet stained nuclei, it is possible for nuclear fragments to be mistaken for bacteria;

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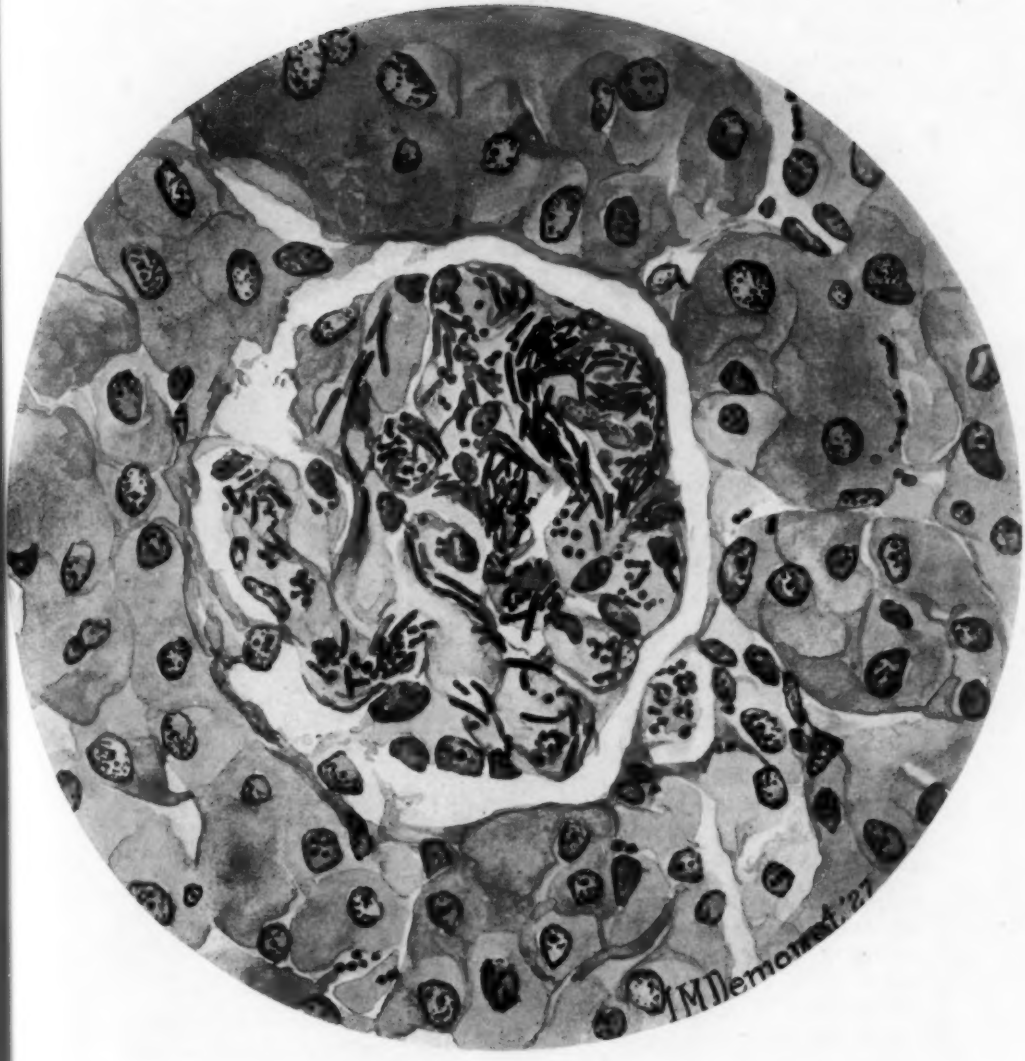
* From the Hygienic Laboratory.

1. Gram, C.: Fortschr. d. Med. **2**:185, 1884.

2. Weigert, C.: Ztschr. f. wissensch. Mikr. **4**:511, 1887.

3. Mallory and Wright: Pathological Technique, ed. 8, Philadelphia, W. B. Saunders Company, 1924.



B. anthracis in kidney of a guinea-pig.

also, it remains uncertain, at least in my mind, whether the gram-negative bacteria have been decolorized when the tissue elements retain the violet stain.

In this connection it should be noted that Kemp and Fleisher [4] found aniline a satisfactory differentiating medium for the Gram stain for bacterial smears, citing a list of only nine organisms on which they tried the method. Their method, requiring heat drying after the aniline, cannot be regarded as applicable to tissues.

In an attempt to overcome these objections I tried the use of acetone as a decolorizing and dehydrating agent, and found that the violet stain was promptly and completely removed from the tissues; that gram-positive organisms retained the violet stain; that a safranine or basic fuchsin counterstain could then be used and dehydration and clearing accomplished by means of acetone followed by xylene, and that the whole process took about three minutes, from the removal of the paraffin to mounting in balsam.

The use of acetone as a differentiating reagent in the Gram stain was first mentioned by Kisskalt [5] in 1901, who found that it decolorized the bacteria. Lyon [6] in 1920 again tried acetone and obtained favorable results. He mentioned colon bacillus and staphylococcus as test objects, but doubtless tried this reagent on other organisms. Burke [7] (1921) and Kopeloff and Beerman [8] (1922) found acetone satisfactory. Hucker and Conn [9] (1923) found that the results following the use of acetone were less constant than those after alcohol, but I do not know whether the organisms used included the common pathogens or not.

To determine the effects of alcohol and of acetone on various of the common pathogenic organisms, I made smears of twenty-four hour cultures; stained them with ammonium oxalate crystal violet (modified from Hucker's second formula: crystal violet, 2 Gm.; 95 per cent alcohol, 20 cc.; 1 per cent ammonium oxalate in distilled water, 80 cc.) for thirty seconds; washed them; applied Lugol's solution (1:2:100) for thirty seconds; washed them; then differentiated one smear from each culture with alcohol and one with acetone in each case until no more color was removed; washed them; counterstained them with 0.5 per cent safranine for thirty seconds; washed them, and dried them.

In the case of the acid-fast bacilli, staining for one minute with crystal violet was found to give better results than staining for thirty seconds. The results appear in the table.

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4. Kemp, H. A., and Fleisher, M. S.: J. Lab. & Clin. Med. **11**:575, 1926.

5. Kisskalt, C.: Centralbl. f. Bakteriol. **30**:281, 1901.

6. Lyon, M. W.: Acetone as a Decolorizer in Gram's Staining Method, J. A. M. A. **75**:1017 (Oct. 9) 1920.

7. Burke and Ashenfelter: Stain Technology, **1**:63, 1926.

8. Kopeloff, N., and Beerman, P.: J. Infect. Dis. **31**:480, 1922.

9. Hucker, G. J., and Conn, H. J.: Technical Bulletin no. 93, N. Y. Agric. Exper. Sta., Geneva, N. Y., March, 1923.

Results of the Gram Stain on Smears of Twenty-four Hour Cultures in Which Alcohol and Acetone Were Used as Decolorizing Reagents *

Organism	Alcohol	Acetone
B. subtilis	± (few +, mostly —)	+ (10-20% —)
B. subtilis	+ (few —)	+ (moderate number —)
B. anthracis	+ (occasional —)	+ (few —)
B. anthracis, isolated 8/8/19	+ (few —)	+ (few —)
B. anthracis, avirulent	+ (few —)	+ (few —)
B. anthracis, Lloyd 5/11/15	+ (occasional —)	+ (occasional —)
B. anthracis, Seattle, 1922	+ (few —)	+ (few —)
B. tetani, No. 247	+ (50% —)	+ (50 % —)
B. tetani, No. 248	± (mostly —)	± (mostly —)
B. tetani, Tulloch, No. 1	∓ (occasional +)	± (about 10% +)
B. tetani, Tulloch, No. 2	— (few + spores)	± (about 10% +)
B. tetani, Tulloch, No. 5	—	∓ (occasional +)
B. tetani, old strain	—	∓ (few +)
B. chauvei, Hopkins	+ (20-30 % +)	+ (few —)
B. chauvei, McFarland	— (few spores +)	± (10% +)
B. botulinus	— (few spores +)	∓ (few +)
Vibrion septique	∓ (occasional +)	— (few spores +)
B. diphtheriae	+ (occasional —)	+ (few —)
B. diphtheriae, Park, No. 8	+	+
B. diphtheriae, isolated 4/11/24	± (some + granules)	+
Diphtheroid, R. C., from lymph gland	+	+
B. acidophilus (milk)	+ (40-50% +)	+ (50-60% +)
Monilia psilosis	+ (many; some —)	+ (about 40% +)
Monilia psilosis, isolated 1/8/18	+ (many partly +, some —)	+ (about 50% + few mixed)
Monilia psilosis, No. 93, Porto Rico	+ (many partly +; 27% —)	+ (about 40% +, few mixed)
B. coli	—	—
B. proteus vulgaris	—	—
B. enteritidis	—	—
B. typhosus	—	—
B. typhosus, Navy Medical School	—	—
B. paratyphosus A	—	—
B. paratyphosus B	—	—
B. dysenteriae, Shiga	—	—
B. dysenteriae Flexner Strong	—	—
B. pyocyaneus	—	—
B. pestis	—	—
B. abortus	—	—
B. melitensis	—	—
B. tularense	—	—
B. prodigiosus	—	—
B. pseudotuberculosis, rodentium	—	—
B. pseudotuberculosis, rodentium, No. 111	—	—
B. pseudotuberculosis, rodentium, No. 105	—	—
BA (pleomorphic bacillus from bubo)	—	—
Vibrio cholerae	—	—
Staphylococcus aureus, old strain	+ (occasional —)	+ (few —)
Staphylococcus aureus, No. 600 (first subculture)	+ (40% +)	+ (70% +)
Staphylococcus aureus, No. 600 (sixth generation on agar)	+ (few —)	+ (occasional —)
Staphylococcus albus, R. B. (first subculture)	+	+
Staphylococcus albus, R. B. (eighth generation on agar)	+	+
Staphylococcus albus, NA (recent isolation)	+ (few —)	+ (occasional —)
Staphylococcus aureus (Pasteur Institute)	+	+
M. tetragenus	+	+
Streptococcus viridans	+ (occasional —)	+ (occasional —)
S. viridans	+	+
S. erysipelatis	∓ (few +)	+ (few —)
S. hemolyticus	+ (50% +)	+ (few —)
S. hemolyticus	—	∓ (few +)
S. hemolyticus, 7Cl (guinea-pig pneumonia)	+ (few —, many ±)	± (few +, many ±)
S. scarlatinae, Dick II	—	+ (about 25% +)
Pneumococcus	+ (about 20% +)	+ (about 80% +)
Pneumococcus	+ (about 20% +)	+ (about 80% +)
Meningococcus	—	—
B. leprae, rat	+	+
B. leprae (human) No. 361	+	+
B. leprae (human) No. 362	+ (few —)	+ (few —)
B. leprae (human) No. 364	+ (10% —)	+ (10-15% —)
B. leprae (human) No. 365	+	+ (few —)
B. leprae (rat) No. 366	+ (few —)	+
B. leprae (rat) No. 368	+ (few —)	+ (occasional —)
B. leprae (human) No. 370	+ (few —, many ±	+ (few —)

* The cultures of the acid-fast group were from four to six weeks old.

Results of the Gram Stain on Smears of Twenty-Four Hour Cultures in Which Alcohol and Acetone Were Used as Decolorizing Reagents—Continued

Organism	Alcohol	Acetone
B. leprae (human) No. 430	+ (few —)	+ (few —)
B. tuberculosis, BCG	+	+
B. tuberculosis (bovine) No. 523	+	+
B. tuberculosis (bovine) No. 444	+	+
B. tuberculosis (bovine) No. 444 (old)	+ (many —)	+ (beading)
B. tuberculosis (human) H37	+	+
B. tuberculosis, avian	+	+
B. tuberculosis, ranae	+ (few —)	+ (20% — and ±)
B. tuberculosis, Friedmann-turtle	+	+
B. smegmatis	+	+
B. stercussis (mist bacillus)	+	+
B. phlei (timothy bacillus)	+	+

On comparing the results in this table, it is readily seen that the reactions are at least comparable following the use of the two reagents, and that when discrepancies exist, the results after acetone are more often nearer to the accepted reaction for the organism in question. In practice the acetone method is easier and gives sharper results, because all the macroscopic color that is going to come out is extracted in the first five to fifteen seconds.

Surgeon W. T. Harrison rechecked the results on the smears of some forty of these organisms.

TECHNIC

The method for staining gram-positive bacteria in sections is in detail as follows:

Paraffin sections of about 5 microns thickness or frozen sections fixed to the slide by the celloidin method (Mallory and Wright[3]) are brought down to water in the usual way.

1. The sections are stained for thirty seconds with ammonium oxalate crystal violet.[10] For tubercle and lepra bacilli, staining for a longer period or heating is often necessary. Heating for ninety seconds on a hot plate at from 50 to 52 C. has been found satisfactory.

2. The sections are washed in tap water.

3. Lugol's solution I:KI: H_2O=1:2:100 is applied for thirty seconds.

4. The sections are washed in tap water.

5. Acetone (from dropping bottle) is applied until no more color is removed (about ten to fifteen seconds).

6. The sections are washed in water (they should not be allowed to dry after the acetone is applied).

7. They are counterstained with 0.5 per cent safranine in water for thirty seconds.

8. They are washed in water.

9. They are dehydrated and differentiated with acetone. (A certain amount of red comes out in this process, leaving the cell nuclei deep red, and the cytoplasm pink).

10. They are cleared with xylol (in moist weather it may be necessary to blot off the xylol once with filter paper as the acetone is quite hygroscopic).

10. Crystal violet 2 Gm.; 95 per cent alcohol 20 cc.; 1 per cent ammonium oxalate in distilled water 80 cc. The preparation is filtered after it has dissolved. It keeps well.

Gram-positive bacteria are blue black; gram-negative organisms, red; cell nuclei, deep red; cytoplasm of lymphocytes and plasma cells, moderately deep pink; cytoplasm of other cells, pale pink; fibrin, pale pink; collagen, usually pink, sometimes light violet in dense bundles.

The method was used on the following tissues with results as noted:

1. Disseminative tuberculosis, in man; formalin fixation. Occasional slender gram-positive rod in caseous tubercles in spleen.

2. Disseminative tuberculosis (acute), in monkey; Zenker formol fixation. Liver abscess showing numerous acid-fast bacilli by Ziehl Neelsen method showed equally numerous slender, beaded gram-positive bacilli.

3. Leprosy, in human being (I am indebted for this material to Acting Assistant Surgeon O. E. Denney in charge of U. S. Marine Hospital at Carville, La., National Leprosarium). Four sections of spleen, three of liver and two of testis showed beaded gram-positive bacilli in all, and in distinctly greater numbers than with the Ziehl Neelsen stain. Six of seven sections of skin nodules, in only one of which bacilli were demonstrated by the usual acid-fast method, showed a few gram-positive rods. It was found necessary to heat this material in the crystal violet to secure staining.

4. Acute appendicitis, in man; formalin fixation. Sharply blue black diplococci and few red bacilli in pus in lumen.

5. Acute diffuse appendicitis, in man; formalin fixation. Fibrinopurulent exudate toward lumen, loaded with blue black cocci in pairs and short chains. Fibrin red.

6. Acute hemorrhagic appendicitis, in man; formalin fixation. Blue black cocci in short chains in detached tissue fragments in lumen.

7. Acute diffuse appendicitis, in man; formalin fixation. In ulcerated areas short chain streptococci and some large bacilli retained the stain, while a few gram-negative bacilli also were stained.

8. Acute appendicitis, in man; formalin fixation. Blue black diplococci in pus, in bases of ulcers, and occasionally beneath intact epithelium.

9. Subacute tonsillitis, in man; formalin fixation. Blue black cocci and mold colonies in crypts.

10. Organizing pneumonia, in guinea-pig; alcohol fixation. Blue black diplostreptococci in alveoli, extracellular and intracellular in pus cells (this organism isolated in pure culture, found pathogenic for mice and recovered again from mice).

11. Late organizing pneumonia, in guinea-pig. Few alveoli still filled with pus and gram-positive cocci in pairs and short chains.

12. Pneumonia, gray hepatization in monkey; Zenker formol fixation. Space between leukocytes in alveoli packed with minute red rods (possibly influenza).

13. Terminal bronchopneumonia, in man; formalin fixation. Early red hepatization. Blue black short chain streptococci and large capsulated bacilli, red small slender bacilli in alveoli (case of acute nephritis).

14. Plague pneumonia, in human being (Los Angeles outbreak). Many short thick gram-negative bacilli in alveoli.

15. *B. tularense* in mouse liver. Pale gram-negative bacilli in swollen liver cells.

Neither *B. pestis* nor *B. tularense* is particularly well stained by this method.

16. Experimental staphylococcus infection of subcutaneous tissue in guinea-pig. Acute sanguinopurulent inflammation with numerous gram-positive staphylococci in lesion, many phagocytosed and in varying phases of disintegration.

17. Anthrax in guinea-pig; Zenker formol fixation. Few typical blue black rods in various tissues.

18. Anthrax in guinea-pig; Zenker formol fixation. Tissues loaded with typical blue black rods. Tissues all in varying shades of red as may be seen in the plate. Also some red bacilli (the results of culture smear on this same stain should be compared).

SUMMARY

1. A table of the reaction of various organisms to Gram staining, with alcohol and acetone used as decolorizing reagents, is given.

2. A method of staining gram-positive bacteria in tissues is given.

3. This method can be carried out in less than three minutes, and it gives clearcut results.

A SIMPLIFIED METHOD FOR THE CULTIVATION OF ANAEROBES IN FLUID MEDIA*

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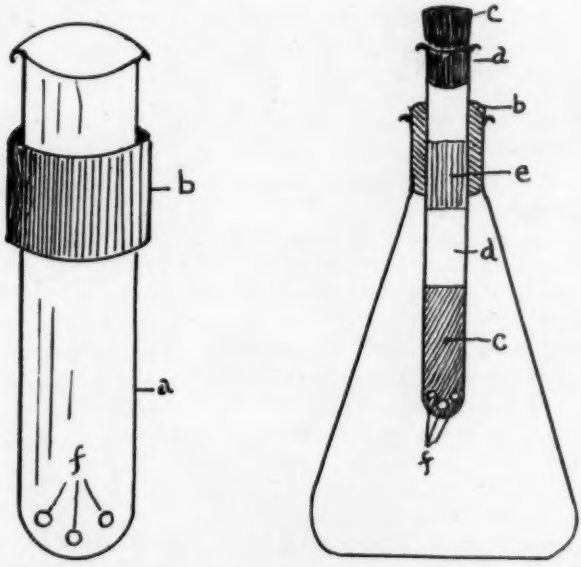
The prevailing method for making anaerobic cultures in fluid media is a long drawn out procedure, requiring much time for the preparation of the cultures and considerable room in the incubator. The following method, which is offered only as a suggestion, may after trial and modification develop into a simple method of some value.



Apparatus used in cultivation of anaerobes in fluid media.

The method is chiefly centered on an absorption tube (*a*) shown in the illustration, which can be prepared by any laboratory worker. Five or six holes (*f*) 2 mm. in diameter are made on the lower end of a tube that is from 10 to 12 cm. long and 2 cm. in diameter. The tube is well packed about one-third

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*From the Research and Clinical Laboratory of the Trudeau Sanatorium.

with cotton (*c*). A rubber tubing (*b*), with an inside diameter of 20 mm., an outside diameter of from 25 to 26 mm. and 30 mm. long, is slipped over the absorption tube. The thickness of this tube will depend on the size of the mouth of the culture flask. The tube is then wrapped in paper in the usual way, sterilized at 15 pounds pressure and kept until needed. The broth media is inoculated as usual. The cotton plug of the flask is aseptically replaced with the absorption tube. Pyrogallol is placed in the tube (*d*) on top of the cotton packing (*c*). Ten per cent sodium hydroxide (*e*) is then slowly poured into the tube over the pyrogallic acid until the cotton packing (*e*) is well dampened. An excess must be avoided. The absorption tube is then closed with a rubber stopper and the connections well sealed with paraffin.

A RAPID METHOD FOR DECALCIFICATION*

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AND
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In the study of rickets and other diseases of the osseous system, the preparation of sections for histologic study is of utmost importance. However, the methods now employed are prolonged and tedious, so that many laboratories dispense with microscopic examinations of the tissues and rely on gross appearances, roentgen-ray examinations or chemical analysis of the bone ash. This fact leads to much confusion and to discrepancies in the literature on rickets, for there are other diseases of the bone that simulate rickets in macroscopic appearance and ash content, and yet that present a histologic picture entirely different from that of true rickets.

The usual time necessary for complete decalcification with Müller's solution is from six days to eight weeks, depending on the size and hardness of the bone. With acids, somewhat less time is needed. However, the use of acids is not desirable and at times is contraindicated, as it tends to swell the tissues, requires continuous washing and may interfere with staining.

While working on the effect of sodium citrate on the dialysability of serum calcium,[1] we noticed the affinity of citrates for calcium and the formation of a soluble, slightly dissociable calcium citrate. This suggested the use of sodium citrate as a decalcifying agent. The decalcifying solution we use consists of: 1. Formaldehyde (10 per cent) 100 cc. 2. Sodium citrate, 20 Gm. This solution causes rapid decalcification and, at the same time, has the advantage of being a fixing and decalcifying agent.

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*From the Harry Caplin Pediatric Research Laboratory of the Jewish Hospital.

1. Shelling, D. H., and Maslow, H. L.: To be published.

TECHNIC

Fairly thin sections of bone, either fresh or previously fixed in formalin, are placed in this fluid and allowed to stand from two to three days, after which time complete decalcification is determined by the absence of grating when the specimen is teased with the point of a needle. The specimens are then washed, dehydrated, embedded, cut, stained and mounted in the usual manner.

SUMMARY

Decalcification can be accomplished quite rapidly with sodium citrate.

The sodium citrate may be dissolved in formalin and the solution used for fixing as well as decalcifying.

It does not interfere with the ordinary staining methods.

General Review

ELECTROPATHOLOGY

A REVIEW OF THE PATHOLOGIC CHANGES PRODUCED BY ELECTRIC CURRENTS *

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CONTENTS

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INTRODUCTION

Ever since the discovery of electricity its action on the living organism has attracted the interest of biologists and physiologists. Crude experiments date back nearly 150 years. The first fatal accidents followed the introduction of the dynamo machines for producing electric energy. According to Jex-Blake, a stage carpenter was killed in 1879, at Lyon, by an alternating current of 250 volts. The next year a man died near Birmingham after an electric shock. In 1882, Brouardel, in Paris, performed an autopsy on a man whose death was caused by his touching a live wire of 250 volts alternating current. In the same year, an engineer was killed at Triest by a direct current of 500 volts.

With the rapid development of the electric industry the number of accidents has risen to a considerable height, although it has not paralleled the extensive use of electricity in daily life. Calculated per mile of live wire, the number of accidents during the last years has even decreased.

Exact information of the yearly number of electric accidents is difficult to obtain. Minor injuries often will not be reported, and severe accidents, and even cases of death, sometimes go under another name since the circumstances under which they were contracted were doubtful and exact postmortem examinations were not performed. Taking Switzerland as an example, a small country with a large electric industry, one finds that 969 persons were injured by electric currents during the years 1903 to 1921. In 1904, forty-six accidents occurred, and in 1920, ninety-eight accidents occurred. Naville and de Morsier report that in France about 300 electric accidents occur annually. According to Boruttau, from 1906 to 1915, 220 people were injured by high tension currents in Germany; most of them died. In England and Wales, 183 deaths due to electricity were reported during the years 1901 to 1910. Jex-Blake gives the number of people killed by electricity, annually, in all Europe, as 200. The number of electrical fatalities in the United States over a period of ten years is given in table 1.*

The relation of the death rate from electricity (lightning excepted) to that from other causes is given in table 2.

There are two avenues of approach to the problem of injuries and deaths caused by electricity, namely, experiments on animals and studies on human accidents. The first scientifically conducted experiments were performed in France by Brouardel, Gabriel and Grange (1884) and by Brown Sequard and d'Arsonval (1886-1887), and in this country by Brown, Kennelly and Peterson in Edison's laboratory (1889). The

* Tables 1 and 2 are taken from: Fatal Accidents from Electric Shock in Recent Years in the United States and Canada, in England and Wales, and in Switzerland: A Report by the Engineering Committee of the Conference on Electric Shock, J. Indust. Hyg. **10**:110, 1928.

latter experiments preceded the first legal execution in the state of New York in 1890. In 1899, Prevost and Battelli, in Switzerland, and Cunningham, in the United States, published extensive and excellent investigations on various animals. Among succeeding papers on experimental electric shock are those of Boruttau, Cluzet and Bounamour, Crile and Macleod, Jellinek, Kawamura, Pietrusky, Rodenwaldt, Urquhart and Weiss. They added many details, but, in the main, confirmed the results of Prevost and Battelli and of Cunningham.

Interesting and elucidating as these experiments on animals are, there is one objection to them which diminishes their value; namely, the great differences among the various species of animals regarding their sensi-

TABLE 1.—*Number of Electrical Fatalities in United States Over a Period of Ten Years*

Year	Number of Deaths	Death Rate per 100,000	Year	Number of Deaths	Death Rate per 100,000
1915.....	515	0.8	1920.....	822	0.9
1916.....	586	0.8	1921.....	741	0.8
1917.....	654	0.9	1922.....	842	0.9
1918.....	754	0.9	1923.....	945	1.0
1919.....	748	0.9	1924.....	975	1.0

TABLE 2.—*Relation of Death Rate from Electricity (Lightning Excepted) to that from Other Accidental Causes*

U. S. Registration Area for 1920

Cause	Death rate per 100,000
Absorption of deleterious gases	3.4
Traumatism in mines	2.5
Traumatism in quarries	0.1
Traumatism by machines	2.5
Railroad accidents and injuries	7.3
Street car accidents and injuries	2.0
Automobile accidents and injuries	10.4
Electricity	0.9

bility against the electric currents. Thus, horses (Arloing) and dogs (Prevost and Battelli) are readily killed by relatively small quantities of electricity. Rabbits (Kawamura), and especially rats (Prevost and Battelli), are much more resistant. Industrial currents are practically nonlethal to frogs and turtles (Cunningham). Unfortunately, only one experiment has been conducted on a monkey (Jellinek). It was more resistant than the dog. One must, therefore, be careful in drawing conclusions from observations obtained in animals as to the mode of human accidents; and the study of cases of electrocution in human beings remains the most valuable source of information. Complete clinical examinations immediately after the accident and scientifically conducted autopsies are of the greatest importance. The literature which has accumulated concerning injuries due to electricity and the causes of

death by electricity is extensive. Many publications are merely reports of cases. There are still many unsolved problems which are attractive to both clinicians and pathologists. In the following pages I shall report what is known at present of the injurious action of the electric currents. Only injuries produced by industrial currents will be considered; those caused by lightning will not be included in this paper.

THE PHYSICAL PROPERTIES OF ELECTRIC CURRENTS WHICH DETERMINE THEIR BIOLOGIC ACTION

The Tension (Voltage).—It is a general custom to distinguish between low tension currents and high tension currents, according to their electromotoric power. Usually 1,000 volts are taken for the borderline. Currents of from 100 to 250 volts are used for supplying houses and work shops with electric energy. High tension currents up to 100,000 volts transmit electric energy over long distances. Some electric railroads use currents of more than 10,000 volts. The modern roentgen-ray machines, in particular those for deep therapy, are built for from 20,000 to 200,000 volts. Currents of medium tension between 400 and 600 volts drive street cars and subway, elevated and suburban trains.

Low Tension Currents: The opinion still prevails among electrical engineers and physicians that low tension currents are not dangerous. This, however, is not true. A current of 100 volts may prove fatal while a shock of 10,000 volts is sometimes survived. The external destructions are much more extensive when a person is exposed to high voltages than when a current of 100 to 200 volts passes his body. The electric arc which usually leaps from the conductor to the body in high tension accidents has a temperature of from 2,500 to 3,000 C., and melts even bone. There may also be differences in the action, certain organs being affected by currents of high voltage, others by currents of a low tension. But this is still doubtful, as far as human beings are concerned.

It will be shown later that several physical properties, besides the tension, determine the detrimental action of electric currents. It is a great mistake to put the danger limit at from 300 to 500 volts. Jellinek says that currents of more than 25 volts should be considered dangerous. He observed a fatal accident in Vienna caused by a current at 60 volts. In the case reported by Capello and Pellegrini the tension was even lower, 46 volts. Jex-Blake speaks of 65 volts as being dangerous when the current passes through the heart. Of the 300 electric accidents which occur annually in France, 100 are caused by currents at low tensions In Switzerland, accidents caused by low voltages seem to be more common than those caused by high tensions. Kawamura, who studied 110 electric accidents in the Mitsui mines of Japan, found that sixty-nine persons were injured by currents of low tensions and forty-one by cur-

rents of high tensions. Schridde saw thirty-seven fatal accidents caused by alternating currents of from 220 to 250 volts.

The most common cause of electric accidents due to currents of low voltage is electric lamps. Poor insulation makes the setting or the handle of the lamp a conductor. In the older literature, attempts have often been made to explain accidents occurring in the handling of electric lamps on the basis of leaking transformers (Jones) or crossed wires which allowed high-tension currents to enter the lamps (Paine), although such cases have never been proved. Such an explanation is not necessary at present. When a person is well grounded and touches a charged part of an electric lamp with his hand, the current will pass through his body. Good grounding is responsible for so many accidents which occur in bath tubs and in the open air on rainy days. Langlois reports the case of a young girl killed in a bath tub as the result of touching a radiator, which, owing to faulty insulation of a live wire, was charged with a current of 110 volts. The same author observed another fatal accident in a bath tub caused by a current of 95 volts. Renon, Kraemer, Jellinek, Witas and others had similar experiences with electrocutions in bath tubs. The death of two people occurred in the subway station Odeon of Paris. They tried to screw in electric bulbs while standing in water. Duncan relates how a powerful young man was killed by an alternating current of 250 volts. Heavy army shoes with steel heels secured excellent grounding. Good grounding during work in a boiler and the handling of a poorly insulated drop light resulted in death in the cases described by Balthazard, Ziemke and me. Jellinek recently wrote an interesting monograph on the dangers of the radio. A woman was killed in London this year by an alternating current of 250 volts. She was listening in with a head phone when she reached for a defective electric bed lamp. The current entered her body through the left hand and left the body through the steel trimming of her spectacles, between which and the poorly insulated head phone, electric sparks had formed. Fatal accidents due to currents of from 100 to 200 volts have also been reported by Balthazard, Balthazard and Dervieux, Cattani, Derome, Fagnet, Fürth, Heydrich, Jellinek, Magnamini, Mohfelt, Tovo, Weber, Weissenrieder and Witas. Zimmern observed burns of the third degree on the fingers, and a fracture of the wrist of the right hand, in a woman who tried to fix an electric curling iron. Rosenberg saw superficial burns caused by an electric pad that had been used in connection with wet dressings. Schwart's paper deals with electric shock in treatment of the scalp.

In the group of accidents due to currents of low tension belong also those that happen during the therapeutic application of electricity. The so-called sinusoidal currents proved dangerous (Boruttau, Meinhold, Meyer, Aschoff, Lewandowsky and others). Sinusoidal currents are

alternating currents with a small number of periods, which pass into each other gradually, without intervals (Boruttau). They are said to cause less unpleasant sensations than common alternating currents. Since Meinhold's first publication in 1913 concerning a death due to sinusoidal current, ten similar cases have been reported. A twelfth, but unpublished, case was that of a man on whom I performed an autopsy. A man, aged 44, with a neurosis, collapsed and became pulseless the moment the electrode was placed on his lumbar region. Artificial respiration was applied for several hours without success. Before starting the treatment the physician had tried the current on himself without ill effect. The tension used in all these cases did not surpass 50 volts and was usually less, about 30 volts.

From these observations, two conclusions can be drawn, namely, that factors other than the electromotive force of the current are of great importance in the causation of death due to electricity and that great individual differences exist among human beings with regard to their resistance against electricity. A peculiar disposition of the patient or preceding diseases, chiefly of the heart, have been blamed for the unlucky outcome of electrotherapy. This question will be taken up in some detail in connection with the internal factors of death caused by electricity.

High Tension: The possibilities of accidents with high tension currents are too many to be discussed here in detail. Much information can be obtained from a book of Jellinek on accidents due to electricity. The voltage lies anywhere between 1,000 and 200,000 volts. In these accidents, too, grounding is much more common than bipolar connection. In reading the reports of accidents in electric power plants and transforming stations, one is surprised to find how many people were killed standing on iron steps or landing points, or clinging to a metal rail around the generator. These accidents could have been avoided if the rails, steps, etc., had been covered by some insulating material such as rubber, porcelain or hard wood. Good grounding also is found in most of the accidents in roentgen-ray laboratories. Floors in these rooms still are often made of concrete. Concrete, and especially reinforced concrete, are good conductors. Hemler says that grounds are concerned in two thirds of all dangers from electricity in roentgen-ray work. According to Shearer, grounding of the roentgen-ray machines never secures a good protection from injuries due to electricity. Jellinek recommends the wearing of rubber boots in roentgen-ray rooms. Another mode of accidents in roentgen-ray work is the connection of the body between the low and high tension live wires. Polgár reports such a case in which a physician was killed by a current at 40 kilovolts. Touching of the cathode neck and of the anode of a roentgen-ray tube caused

the death of a physician and a nurse, according to an observation of Wetterstrand. The current had a tension of 40 kilovolts.

Electric currents of high tensions also have been used with intention to kill. There are cases of attempted suicide by means of high voltage currents. Gey described a boy, aged 15, who had tried to kill himself by touching a live wire containing 8,000 volts. He recovered from the shock, but lost his right arm. Chiari performed an autopsy on a man who tried to commit suicide by seizing a live wire containing 4,000 volts. He survived the attempt, but died later from tetanus. In order to complete this list I mention the electrically charged wire fences used in the late wars in defense lines and around prisoner camps, and execution in the electric chair (Werner, Blue, Klein, Marvin, Marine and MacDonald).

Intensity (Amperage).—The intensity (amperage) of an electric current in a given conductor is its tension divided by the resistance of the conductor, in the case of electric shock, the human body. The intensity gives, therefore, a more accurate account of the action of the current in the body than the tension. In animal experiments the number of amperes can easily be determined by connecting an ameter in series. Such experiments on dogs were performed by a French commission in 1910 under the direction of Dr. Weiss of the Académie de Médecine. They found that from 70 to 80 milliamperes were sufficient to cause an irreversible stopping of the heart. Higher tension may produce a rigid contraction of the myocardium as part of a general muscular spasm. From this contraction, the heart may recover spontaneously (Naville and de Morsier). Chapuis states that for normal human beings direct circuits of from 200 to 250 milliamperes and alternating currents of from 70 to 80 milliamperes are dangerous. If the resistance of the skin is less than 1,200 ohms, an alternating current of 110 volts can be fatal, since the intensity in the organism amounts to 90 milliamperes.

For treatment with sinusoidal currents, the electrodes are moistened with saline solution. The resistance of the skin may thus be reduced to 300 ohms. A current of 30 volts, then, will be sufficient to reach inside the body the dangerous 100 milliamperes (Boruttau). Many people, however, stand the treatment without any disturbances, and only a few patients have been killed. Jellinek says that the experiences in accidents due to electricity in human beings speak against the danger limits obtained in animals. Unknown biologic facts make certain persons apt to react to low intensities with a definite paralysis of the heart. In electrocutions with from 1,200 to 1,700 volts, 7 amperes were reached. The wet sponge on the head and right calf secured an excellent contact with a low resistance.

In accidents to human beings, only the number of volts can be determined exactly, because the resistance of the body at the moment of the accident is unknown and cannot be reconstructed.

Type of Current.—From the discussion on the relations between the tension and the intensity of the current and its biologic action, it has already become apparent that differences exist between alternating and direct currents. Prevost and Battelli and Peterson were among the first to find that direct currents, ceteris paribus, are less dangerous than alternating currents. Boruttau says that of his 212 fatal accidents only 8 were caused by direct currents. Jex-Blake thinks that direct currents of less than 220 volts seldom prove fatal. According to Chapuis, an alternating current is about three times as dangerous as a direct one of the same voltage.

The number of cycles per second of an alternating current are of great importance. Alternations between 39 and 150 are most dangerous (Galinard). These are the alternations most commonly found in industrial currents. With an increasing number of cycles the dangers of the current become less. The cardiac muscle is about twenty times as tolerant to an alternating current of 1,720 as to a current of 150 cycles (Prevost and Battelli). Tesla, in 1891, made the statement that with a high frequency rate large quantities of electricity are harmless. D'Arsonval found that from 400,000 to 1,000,000 cycles up to 3 amperes have no effect. Human nerves and muscles are insensitive to such high frequencies. The nerve stimulation of one alternation does not have time to register an effect before it is annulled by the next succeeding alternation (Kennelly). High frequency currents are used in modern physiotherapy in the form of diathermy (Nagelschmidt). According to Binger and Christie a diathermy current is a current with approximately 20,000 to 40,000 volts, from 1 to 2 amperes and about 1,000,000 cycles per second.

Farradic currents are nonfatal because of their low intensity (Galinard).

THE PASSAGE OF THE CURRENT THROUGH THE BODY

The Resistance of the Body.—In entering and leaving the body, the electric current encounters the high resistance of the skin, which is surpassed only by that of the bone. Compared to the skin the resistance of the underlying structures and of the internal organs can be neglected.

The Skin: Estimations of the resistance of the skin vary within wide limits. Several factors determine the resistance: first of all, the size, shape and nature of the electrodes. With increasing size of the electrodes, the resistance decreases. Electrodes which fit to the surface of the body also help to diminish the resistance. In accidents, the contacts are usually poor. The electrodes touch only a small area of the skin, and in high tension accidents the contact is often imperfect, a layer of air being interposed between skin and conductor. This layer is

crossed by the formation of an arc in which some of the electromotive force of the current is consumed. Indirect contacts also may result from thin insulating material between conductors and body, such as clothes. Since in many accidents the current leaves the body through the ground, the condition of the footwear is important.

Second, there are great differences in the resistance of the skin, not only between different persons, but between different areas of the same body. The palm is much more resistant than the back of the hand, the skin on the inside of the thigh or the skin of the neck. The callous hand of a workman is penetrated only by currents of high tension. Brandon gives the resistance of the planta pedis with 100,000 ohms per square centimeter. The hard palm of a laborer's hand has a resistance of 1,000,000 ohms, according to Jellinek, occasionally of 2,000,000 ohms. Chapuis states that the resistance of the skin is about 40,000 ohms per square centimeter. Areas with a rich supply of blood vessels and nerves are better conductors. From Galinard's and Kratter's publications one may quote a resistance of 50,000 ohms per square centimeter. An area of 100 square centimeters has a resistance of only 500 ohms. The skin of the thigh of a woman is ten times less resistant than that of a man.

So far, I have considered only dry skin. Sweating may decrease the resistance from 30,000 to 2,500 ohms (Cardieu). Jellinek believes that sweating is a kind of protection, since it directs the current to the surface of the body. Most accidents, however, are observed during the warm periods of the year (Jaeger, Zangger). In water, the resistance of the skin drops to 1,200 and 1,500 ohms.

The question becomes still more complicated by the fact that the resistance of the skin changes during the passage of the current. According to Jolly and Gaertner, it may decrease within one minute from 260,000 to 380 ohms. If burns are formed the resistance will increase even to an extent that the current is broken. Carbonization makes the skin a better conductor.

Other Tissues: From the available literature, the following data are of interest: mucous membranes, 100 ohms (Brandon); muscles, 1,500; brain, 2,000; liver, 900, and bone, 900,000 (Jellinek). Blood is the best conductor, and most of the current passes along the blood vessels (Jellinek).

Total Resistance of Body: This resistance depends, of course, on the distance between the electrodes. It was determined in electrocuted criminals as 218 ohms (Kennelly). With less perfect contacts the values are higher. Jellinek gives it as 50,000 ohms, Bullard (from hand to hand) from 550 to 1,970 ohms and Jelliffe from 610 to 1,870 ohms. In certain diseases the resistance is said to be diminished, especially in exophthalmic goiter and hysteria. Frey and Windscheid and

Boyd make the statement that the resistance of the body is less against alternating currents than against direct currents. An opposite opinion is expressed by Schneider.

The Pathway of the Current.—The electric current spreads radially from the point of entrance, to be collected again at the points at which it leaves the body. The greatest density of the electric field, therefore, is found near the entrance and the exit of the current. Not only is it important whether vital organs such as the brain, medulla oblongata or heart are transversed by the current, but also the amount of electricity to which they are exposed is essential. If, for example, the current meets the heart with its full density, the latter will be much more affected than it would be by the passage of only a few lines. This is sometimes the reason why if two persons are exposed to the same current, one may be immediately killed while the other may survive, without grave injuries. Currents going through the left side of the body are commonly considered more dangerous than those through the right side (Jex-Blake). Kennelly recommends keeping one hand in the pocket when visiting an electric plant. According to Schridde, this should be the left hand. He found in 88 per cent of fatal accidents due to electricity that the entrance of the current was through the left hand. Kawamura's and Jellinek's observations, however, do not support Schridde's statement.

Duration of Contact.—Many authors emphasize the great importance of the time of exposure to the electric current. Contacts which last for several minutes are usually fatal.

THE CHANGES PRODUCED IN THE DIFFERENT ORGANS BY ELECTRIC CURRENTS

The Skin.—In the skin, with its high resistance, the most marked changes are produced. In order to understand these changes one must remember that the effect of the current on the skin is twofold. First, in passing through the skin, the electric energy is transformed into heat. This heat alters the structures along the way of the current. The result is the so-called current marking, which, to a certain extent, is specific and of great diagnostic value. Second, free discharge causes the formation of electric sparks which lead to the formation of burns of the third degree. The sparks may ignite clothes or other things near the body. The flames will produce burns of all three degrees. Usually, one finds a combination of electric burns, with current markings. In high tension accidents, the burns may entirely obscure the typical markings which can best be seen after injury by lower voltages.

The Current Markings: The current markings, as a rule, are formed at the moment the current enters the body, whether the victim survives or is killed (Delbanco). There is no difference in the structure between

alternating and direct currents (Mieremet). This proves that the heat is instrumental in causing the markings and that electrolysis does not play a rôle. In case of direct currents the changes are more pronounced at the point of entrance than at the point of exit of the current (Mieremet). The macroscopic appearance of a typical current mark is as follows: The shape is round, oblong, rosette-like or linear. The diameters vary between a few millimeters and several centimeters. The area is slightly elevated and pale gray, grayish white, yellowish gray or yellow. In the center a crater-like depression is often seen. The relief of the epidermis has disappeared. The hairs are unchanged, even the lanugo hairs remaining intact. The surface frequently shows a negative of the conductor; for instance, a groove of the shape and size of the live wire that caused the contact (Jellinek). The heat makes the horny substances of the epidermis plastic. After cooling, the epidermis hardens, without assuming its original shape (Delbanco). Small metallic granules derived from the conductor may be seen sticking to the epidermis. Iron granules appear dark brown and copper granules yellowish brown. Sometimes the epidermis is missing in places and is found attached to the conductor. The lesion does not smell (Jellinek, Delbanco, Mieremet, Pietrusky, Riehl, Hulst).

A rare type of current mark is described as resembling a bullet wound (Jellinek, Riehl). It is a round hole, penetrating skin, musculature and even bone; it is explained as being the result of the sudden formation of steam in the tissues which finds its way out under high pressure.

In a few instances lesions are found in places other than those which were in direct contact with the conductor. Jaeger observed them around joints and believes that, at the moment of the accident, these joints were bent, giving the current a shorter route through adjacent folds of the skin.

The electric current marking is painless and does not show a surrounding inflammatory reaction (Jellinek). If the patient survives, the altered tissue breaks down slowly, presenting the picture of an aseptic necrosis without pus formation. It seems as if the defense reactions of the tissues had been paralyzed. After demarcation, luxurious granulation sets in, which leaves a thin, pink, smooth scar (Delbanco, Jellinek, Riehl).

The changes under discussion are frequent but not an absolutely constant observation in accidents due to electricity. There are cases in which they are absent and in which no external sign of the electrocution can be detected (Meixner, Fuerth, Jellinek). Schridde failed to find any traces of the current on the skin in one third of his thirty-seven cases.

A case in which I performed an examination several years ago, and which so far has not been reported, shows how important the presence of the current markings can be in revealing the real cause of an obscure death. A plumber, aged 27, was working in a boiler which was standing in a yard. His colleagues outside the boiler noticed that the sound of his hammer suddenly stopped. Since, after several minutes, it did not commence, they looked into the boiler and saw the man lying on his face. When he was removed, he was unconscious and pulseless. Attempts of resuscitation were unsuccessful. The first superficial external examination did not show any injuries, and the air in the boiler was not bad. Hence, it was believed that the man died suddenly from some natural cause. Close inspection, however, revealed a peculiar lesion on the left palm. The skin was thickened and pale gray, and contained several deep impressions crossing each other under a right angle. On both soles two similar smaller areas, without the impressions, were present. The man was barefooted. An electric drop light was found in the boiler. The bulb was protected by a screen of heavy iron wire. One pole of the wire inside the socket touched the brass setting which was in direct connection with the screen around the bulb. The man, no doubt, was holding with his left hand the iron screen which was charged with the current. The current entered the body through the left hand and left it through the feet. It was hot in the boiler, and sweat apparently had diminished the resistance of the skin. The boiler was grounded since it was standing on soil. It was concluded, therefore, that the man had been killed by the alternating current of 220 volts which supplied the drop light.

Lesions due to electricity have also been produced experimentally in rabbits and on the skin of cadavers (Schridde and Beekmann, Rodenwaldt). They were similar to those formed during life.

The histologic picture of the electric current markings has been described by Beekmann, Corin, Delbanco, Hulst, Jellinek, Mieremet, Kawamura, Pietrusky, Riehl, Schridde and Weimann. The stratum corneum is compressed and homogeneous, and stains deeply. Schridde and Beekmann found a superficial carbonization at the positive pole of direct currents. Mieremet, Schridde and Beekmann observed cavities composed of smaller compartments throughout the epidermis. Schridde believes that these cavities, which he calls heat-coombs (Hitzewaben), result from the sudden formation of steam in the epidermis. Delbanco, Jellinek, Kawamura, Mieremet, Hulst and Riehl emphasize the elongation of the cells of the epidermis to long threads. The nuclei of the cells are rod-shaped. The prickle cells are arranged parallel to each other (Delbanco), while the basal cells form tufts (Kawamura). Riehl points out that the long spindle-shaped cells run in various directions forming whirls. A radiation of the cells from a certain point is

typical of the changes produced by cauterization. The stretching of the cells apparently is due to the drying effect of the heat (Hulst). Corin noticed groups of well preserved red cells in the epidermis. The epidermis is often separated from the cutis (Mieremet). In the cutis the papillae are flattened (Kawamura) and the collagenous fibers stain deeply and are thick (Mieremet, Hulst, Schridde, Delbanco). Delbanco speaks of a coagulation of the collagen. Balkhausen and Grueter and Corin found the cutis hyperemic. Pietrusky observed a peculiar contraction of the blood vessels near the center of the lesion. Changes are not seen in the subcutis, since it is a good conductor (Kawamura).

The question as to the specificity of the electric current markings has been answered in a different way. Jellinek and Kawamura are inclined to regard them as typical. Schridde and Hulst do not do so because similar changes have been produced by other methods. Delbanco recalls the experiments of Unna with the small flame of a microburner. Here, too, the prickle cells were transformed to long spindles and the connective tissue fibers of the cutis were thickened. Mieremet, Beekmann and Meixner obtained lesions which closely resembled the electric markings by pressing a glowing platinum or steel wire on the skin.

In spite of these observations the electric current markings remain the most characteristic changes in electric accidents, especially if they are found in places covered by unchanged clothes (Strassmann, Mieremet). In medicolegal cases one must remember that the absence of such changes does not speak against electrocution and that they also may be produced after death. They are the result of a thermic alteration of the tissues, and vital processes do not take part in their formation.

The Electric Burns: Electric burns are characteristic only by their combination with the current markings. An excellent description of electric burns after high tension accidents is given by Besson. The burns form a homogeneous block, uniformly mortified in all parts. They are located in the intact skin like a huge seal. In the center a deep groove extends down to the underlying structures, into the muscles and sometimes even into the bone. The walls of the groove are irregular, black and sometimes covered with deep red islands. As in typical current markings, pain and reactive suppuration are absent. Complications are rare. The demarcation of all the necrotic tissue may lead to severe functional disturbances. Moorhead describes a large scar that followed extensive burns on the back which were caused by an alternating current at 11,000 volts. Six years after the accident, there was still an unhealed area in the center of the scar. The most severe form of electric burns is the carbonization of whole extremities and their complete amputation.

The Electric Edema: In connection with the skin changes, the so-called electric edema is mentioned (Block, Haberda, Jaeger, Jellinek,

Pietrusky, Sandrock and others). This edema is found in fatal accidents, as well as in nonfatal ones. It is usually closely connected with the other skin lesions and is formed within a few seconds during, and immediately following, the passage of the current (Jellinek). The edema is sometimes extensive (Jellinek, Block, Sandrock). Its cause is still undetermined. Jaeger thinks of a venous thrombosis, while Haberda explains it on the base of a local paralysis of the blood vessels. Riehl speaks of a specific alteration of the vascular endothelium. An electric emphysema following an accident due to 16,000 volts of alternating current has been described by Jaeger.

The Voluntary Muscles.—In traversing the body, the industrial currents cause tetanic contractions of the entire musculature (Jellinek). The most severe form of tetanus due to electricity is called by Naville and de Morsier, rigid contraction. Witnesses of accidents caused by electricity often describe how the body of the electrocuted person is bent in extreme opisthotonus. The muscular spasm may be so intensive as to cause ruptures of the muscles (Hackel, Sandrock, Spilsbury), luxation of joints (Jaeger) and even fractures of bones (Zimmern). In some instances, the spasms are restricted to the extremity through which the current enters. A single convolution may fling the body away from the conductor, thus breaking the contact and becoming life saving. On the other hand, the tetanus may fix the victim to the conductor until the current is interrupted.

The severe muscular spasms probably account for the exhaustion and the lasting pains in the muscles often experienced by persons who survive the electric shock.

The tetanic contractions sometimes outlast the passage of the current (Balkhausen and Grueter, M. B. Schmidt and others). In experiments with animals, a similar observation was made by Rodenwaldt. Frommolt and others described a fixation of the hand through which the current had entered in a clawlike position for hours after the accident. Richet has shown that the muscles lose their irritability when passed by alternating currents at high voltages. In fatal cases, the tetanus may pass over directly into rigor mortis. The body then keeps its position after death (cataleptic rigor mortis).

A number of authors have described macroscopic changes of the muscles which extend far beyond the lesions on the surface of the body. Balkhausen and Grueter speak of a resemblance of the muscles to fish meat. Frommolt, in a case of accident by an alternating current at 4,600 volts, found the muscles of the right arm firm, dry, reddish and friable. According to M. B. Schmidt, the microscopic picture in particular, is interesting. There is a displacement of the contractile substance. Instead of the fine cross striation, coarse, hyaline transverse bands are seen. The fibrils pass through these bands which, no doubt,

are composed of the compressed anisotropic disks of the muscle fibers. These are the places of the most extreme and irreversible contraction. According to Schmidt, similar changes are observed in eclampsia. Schaffer saw them in the facial muscles of two persons executed by hanging. Erb described them in 1868, as a result of intensive electric irritation of the muscles. The transverse hyaline bands in the muscles of electrocuted persons were also seen by Balkhausen and Grueter, Frommolt and Lange. Bolognesi produced a disappearance of the cross striation, swelling of the fibrils and, finally, fragmentation of the fibers, in the muscles of rabbits, by low tension alternating currents.

The Bones.—In high tension accidents in which the current enters the body through the skull, lesions of the bone are common (Balthazard, Block, Gerlach, Gubler, Jaeger, Jellinek, Luther, Mason and Lester, Quénu, Reuter, Risel, Sandrock, Schumacher, Stadtmann, Strassmann, Toelker, Wyss, Ziemke). Ranzi, Mayr and Oberhammer observed necrosis of the parietal bone after an accident due to an alternating current from 220 volts and 16⅔ cycles per second.

One would perhaps expect that the current in order to avoid the high resistance of the bone would travel along the soft parts of the scalp. But the bone offers the current a much larger surface than the thin layer of soft tissues which covers it. Most of the current, therefore, will pass through the bone.

In some cases the electric arc burns a deep hole in the bone, and the dura mater and the brain, too, may become affected. In a fatal accident caused by a circulating current of 5,000 volts, Reuter found grayish white, pearl-like globules consisting of calcium phosphate near the body of the victim. There was a large perforation of the skull, with holes in the dura mater and small channels in the brain. Reuter thought that the pearl-like bodies were derived from the bone. He was confirmed in his statement by a second observation in which similar pearls of calcium phosphate were seen attached to the edges of a large hole in the skull. The high temperature of the electric arc had apparently caused a melting of the calcium salts of the bone. The steam of the boiling blood in the diploë dispersed them to small globules.

In other, less severe accidents, the bone is often exposed by the destruction of the soft tissues. This area is dry and yellowish white. If the person survives, the bone thus changed becomes demarcated in from about four to five months. In an observation by Luther, the demarcation was already completed after three weeks. Mason and Lester thought that the deprivation of the periosteum led to the necrosis of the bone. Quénu, emphasizing the fact that bone may live without periosteum, considered the necrosis a direct result of the electric current. He spoke of an electrocoagulation. The high resistance of the bone, no doubt, gives rise to the formation of an intensive heat (Luther).

Either the sequestration is restricted to parts of the bone, such as the tabula externa, or the bone in its entire thickness becomes involved, so that after the sequestration, the dura mater lies free. The prognosis, however, is usually good, and most patients recover. There are a few observations in which the destruction of the bone was followed by the formation of an abscess of the brain in from one to two months after the accident (Jaeger, Ranzi, Mayr and Oberhammer, Mason and Lester).

Because it is impossible to determine the extent of the alteration of the bone right after the accident, conservative treatment is generally recommended. After sequestration has started, the process may be shortened by a trephination in healthy bone (Quénu).

In other bones, too, the electric current may produce severe changes. Ziemke described a fracture of the left humerus as a sequel to an accident due to 5,000 volts. The bone was carbonized and covered by a white porcelain-like mass of calcium phosphate. Jellinek examined the roentgenograms of severely injured long bones. The demarcation starts as a faint line. In some cases a strong formation of osteophytes is present, peripheral to the sequestrum. The medullary cavity may be filled with hard tissue.

The Blood Vessels.—Injuries caused by electricity often show the tendency to progress beyond the changes visible externally immediately after the accident (Wildegans, Blue, Jellinek and others). The apparently healthy tissue surrounding the wound may, to a large extent, become necrotic and break down. Sometimes a whole extremity is transformed gradually into a necrotic mass. The first examination, therefore, does not yield any information as to the extent of the injury, and expectant treatment of electric wounds is recommended by all experienced observers, because it can never be determined whether one is operating in healthy tissue.

The progressive character of wounds caused by electricity seems to be due to an alteration of the blood vessels which may involve large sections of them. Jellinek says that the wall of the blood vessels through which a current has passed is brittle and friable. The endothelium is changed, and parietal thrombi are attached to the intima. The great vulnerability of the vessels accounts for the severe hemorrhages as complications of injuries due to electricity, and also explains the great difficulty often experienced in the ligation of arteries near the wounds.

In microscopic sections, Balkhausen and Grueter found an extensive destruction of the nuclei, especially in the media. Frommolt observed an occlusion of the smaller blood vessels by homogeneous masses in which erythrocytes were not discernible. Martin, Couvert and Dechaume examined the arteries of a lower extremity which had been removed

as a result of severe burns caused by an alternating current from 10,000 volts. The operation was performed eight days after the accident. Their observations were as follows: There was a separation of the elastica interna from the media, with necrosis of the media, and, to a lesser degree, of the intima. The necrosis was considered secondary to the destruction of the elastica. Defensive reactions were insignificant. The lumen was not affected. The authors said that similar changes occurred after exposure to radium.

In the arteries of rabbits, through the legs of which a low tension current had passed, Bolognesi found ruptures of the elastic fibers and a diffuse thrombosis. Pietrusky sent a direct current from 220 volts through an artery of a guinea-pig, and saw an intensive contraction of the vessel, which persisted after the current had been broken.

The Peripheral Nerves.—When a nerve is passed by a strong electric current it loses its irritability and conductivity. This was shown for the frog's nerve by Stern and Battelli. In guinea-pigs, the irritability returns after from three to four minutes.

Anatomic changes of the nerves above the burns were observed in a few cases of injuries due to high tension. Frommolt and Wildegans described the nerves as friable and yellowish gray.

Experimental lesions of the nerves were produced by Bolognesi and Pietrusky. In rabbits, Bolognesi found a swelling and twisting of the axons and a breaking down of the nerve sheaths. Pietrusky observed a fusing together of the nuclei of Schwan's sheaths and of the fibers.

The Central Nervous System.—Some persons retain full consciousness when they meet with an electric accident. They scream for help and are even able to free themselves if the muscular spasms are not generalized. Others drop into unconsciousness without a sound or after a cry at the moment they touch the conductor. In a few instances the victims become unconscious after the current has been broken. In legal electrocution, abolition of consciousness is said to be instantaneous (Mac Donald).

According to Kawamura, unconsciousness is more common in accidents due to currents of high tension than in those of low voltage. His percentages are 63 for the former and 31 for the latter type. Jellinek, who gives extensive casuistics, did not find any marked differences between high and low tension and between direct and alternating currents. Apparently, individual factors are of foremost importance.

Jaeger states that the electric shock is similar to a concussion of the brain. Its severity and duration varies within wide limits. If the victim is not killed or rendered lifeless by the current, consciousness may return after a few seconds (Brandau, Jellinek). Mental functions are not impaired, and the shocked person remembers every detail of the accident. He is able to get up and to resume his work, provided the

injuries inflicted by the contact are not severe. On the other hand, the shock may last for hours and even for days. The unconsciousness sometimes passes into a deep comatose condition which is interrupted by severe convulsions terminating in death. Restlessness is common after electric accidents and there are also some reports of attacks of frenzy. Even after a long period of somnolence, complete recovery may ensue. Block observed retrograde amnesia following a shock caused by a current of 10,000 volts.

The reports on the macroscopic and microscopic observations of the central nervous system in death from electric shock reveal great differences. Jex-Blake thinks that visible lesions are present only when large quantities of electricity pass through the body for a long time. Schmidt, Schridde, Ziemke and others did not find any changes in the brain. Kratter, Kawamura, Capogrossi, Mott and Schuster describe small perivascular hemorrhages, especially in the medulla oblongata and in the floor of the fourth ventricle. These hemorrhages seem to be common after legal electrocution (Werner, Shady, van Gieson). Jellinek repeatedly saw a marked edema of the brain.

Corradi, in 1898, published microscopic studies on the brains of dogs killed by electricity. He described the histologic picture as characterized by a chromatolysis of the ganglion cells, rupture of the cells and dislocation of the nucleoli. In human brains, too, similar lesions were described. Grubler's observations consisted of a loosening of the glia, vacuolation of the nerve cells and a close position of the nuclei to the wall of the cells. Kawamura says that some nerve cells appear normal while others are shrunken and hyaline. In the medulla oblongata the tigroid is broken up to small granules. A destruction of the Nissl bodies was also observed by Capogrossi. Mott and Schuster examined the brain of a man who died seven hours after an electric shock by a current from 20,000 volts. There was a diffuse chromatolysis of the ganglion cells in the cortex and medulla oblongata and the formation of a peculiar intracellular and intranuclear network. Jellinek reports a destruction of the ganglion cells with extrusion of the nuclei. Although these changes are not typical of death due to electricity, most investigators consider them a direct result of the action of the current.

Spitzka and Radasch sectioned the brains of five electrocuted criminals. They depictured peculiar areas, from 25 to 200 microns in diameter around small blood vessels. There was a central rarified zone and a peripheral condensed one. They explained their observations on the basis of a sudden liberation of gas bubbles by the electrolytic action of the current. The currents used, however, were alternating currents, and an electrolytic action under the condition given is not likely. I rather believe that the vacuolation of the brain results from excessive

temperatures. In electrocution, the brain becomes extremely warm. Werner recorded a temperature of 145 F. Since the resistance of the skin is greatly diminished by the wet sponge pressed on the head, much heat is apparently liberated in the bones.

Numerous arguments were brought forward against the significance of the histologic observations under discussion. They were called artefacts or postmortem changes (Rodenwaldt, Rabinowitsch). This question requires further study. Experiments on protozoa have shown that electric currents may cause a complete destruction of the cytoplasm (Davenport). Their action on isolated cells of higher animals has not yet been tested, save for the paralytic effect on the white blood cells. It would be interesting to determine, under the microscope, whether freshly isolated nerve cells lose their specific structure when exposed to currents. It is not necessary that the cells be stained, since observation in ultraviolet light brings out the Nissl bodies and the nuclei almost as distinctly as stains do.

The Eye.—The changes observed on the eyes rather belong to late complications of accidents due to electricity. But since they are, no doubt, a direct result of the currents they may be taken up in this connection. The so-called electric cataract is important. It occurs chiefly in cases in which the current enters the body through the head. Several weeks after the accident the patient notices that he cannot see well. There is a progessing diminution of vision. Examination of the eyes reveals numerous flaky opacities near the anterior capsule and in the deeper layers of the lens. Either both eyes are affected to the same extent, or one eye is more involved than the other (Brunner, Horton, Franklin and Cordes and others). A wide range of voltage may lead to the formation of cataracts (from 220 to 50,000 volts). The earliest case reported was three weeks after the accident, the latest two years after (Streber). Hess noticed extensive changes in the epithelium of the anterior capsule. Enucleation of the lens is generally recommended.

Lesions of the cornea and fundus, without alterations of the lens, were found by Pfahl. Osboren saw an optical atrophy which developed after an accident caused by 5,000 volts. Pfahl finally observed loss of accommodation due to an electric shock from 6,000 volts.

The Heart.—Functional alterations of the heart play an important rôle in the explanation of the mechanism of death from electric shock. As far as animals are concerned, more is known about the action of the electric currents on the heart than on any other organ. In man, however, observations are scanty.

Studies on dogs, cats and other animals have shown that when a current at low tension passes through the heart complete inhibition of the ventricles takes place. The blood pressure rises slightly, then drops

and continues to do so after the current has been broken. Opening of the chest reveals incoordinate twitchings of separate muscle bundles of the ventricles. This ventricular fibrillation has been described by Ludwig and Hoffa, Prevost and Battelli, Cunningham, Weiss, Boruttau, Cluset and Bonamour, Crile and Macleod and MacMillan. While the closing of the current causes an arrest of the heart, its opening is followed by the ventricular fibrillation (Cluzet and Bonamour, Crile and Macleod). The twitching of the fibers starts at the base of the heart. It does not have a mechanical effect and the circulation stops. Blood is not passing through the central nervous system and through the myocardium. Hence, death in dogs is immediate (Sekundenherztod of Hering). The fibrillating dog's heart does not recover. In rabbits, and especially in rats, fibrillation may pass over spontaneously into rhythmic contraction. This is the reason why rabbits and rats are resistant to electric currents.

Severing of the nervi vagi does not influence the occurrence of cardiac fibrillation (Prevost and Battelli). It results, apparently, from a direct action of the current on the muscle fibers or ganglion cells of the heart. For a short time, the auricles may continue beating regularly (Crile and Macleod, Cluzet and Bounamour). Sometimes, they too start fibrillating.

Boruttau says three factors are essential to produce ventricular fibrillation, namely, a sufficient density of the current, a low or medium tension and a certain length of the contact which, however, may be short. Even a current from 1 volt may induce fibrillation when applied directly to the heart. Prevost and Battelli putting the electrodes in the mouth and rectum of dogs produced fibrillation with alternating currents of from 10 to 20 and direct currents of from 50 to 70 volts. The French commission found that an intensity of from 70 to 80 milliamperes is sufficient to kill a dog by cardiac fibrillation. Cluzet and Bounamour used a current from 110 volts. They give an accurate account of the electrocardiagraphic observations. The tracings are characterized by the irregularity and great amplitude of the oscillations. It is impossible to distinguish the ventricular oscillations from extrasystoles. After several minutes, the fibrillation of the ventricles becomes less distinct. There are only a few small contractions, apparently starting from the auricles. The periods between the large oscillations of the cardiogram become longer and longer. After a little while, there is only a sinuous line, with a few small and irregular oscillations. Ultimately, the auricles come to a standstill, and the tracing is a straight line. The electric activity of the heart outlasts its mechanical activity for from five to ten minutes.

High tension currents have a different effect on the myocardium. They do not cause ventricular fibrillation. Prevost and Battelli applied alternating currents at 1,200, 2,400 and 4,800 volts. When the cur-

rent is closed, the heart action stops immediately. When the current is opened, the ventricles start to beat rapidly and strongly, and the arterial pressure rises. Rhythmic contractions continue until paralysis of the respiration leads to a gradual decline of the blood pressure. Naville and de Morsier point out that currents from high tension cause a rigid contraction of the heart which either is permanent or passes into rhythmic action after the current is disconnected.

Prevost and Battelli were able to resuscitate the fibrillating hearts of dogs by means of electric currents at 4,800 volts.

Ventricular fibrillation in accidents caused by electricity in human beings has never been demonstrated (Jellinek). Jaksch and Rihl observed auricular fibrillation for two days after a shock by a current from 220 volts. A slight but distinct dilatation of the left auricle occurred. Electrocardiographic examination showed an arrhythmia perpetua, with 450 auricular and 120 ventricular oscillations per minute. The dilatation of the auricle disappeared on the third day. At this time the electrocardiogram was normal. Laslett observed a paroxysm of auricular flutter in a man who had received a shock from an electric lamp. It disappeared over night.

Most authors who performed autopsies on electrocuted persons were unable to find anatomic lesions of the heart. There are only a few positive statements. Gubler speaks of a loosening of the myocardial fibrils and of small ruptures of the fibers. Kawamura, too, mentions ruptures of the fibers besides recent hemorrhages. A fragmentation of the myocardium is given by Capogrossi as the main observation in the heart of a man who was killed by a current from 50,000 volts. Pietrusky describes a coagulation necrosis of the posterior leaflet of the aortic valve in a man who was fatally injured by a current at 220 volts. The area was reddish brown. In another accident caused by an alternating current from 220 volts, an extensive hemorrhage was found in the same place.

The Kidneys.—The frequent occurrence of albumin in the urine after accidents due to electricity points to an alteration of the kidneys. This alteration, apparently, is not due directly to the trauma caused by electricity, but results from toxic products of an abnormal protein cleavage (Jaeger). Klein found that the urine of four electrocuted criminals contained much albumin. Albuminuria is reported in the cases of Balkhausen and Grueter, Jellinek, Ranzi, Mayr and Oberhammer, Chiaria and others. Casts, too, may be present (Jaeger). According to Jellinek, the albumin usually disappears from the urine during the first three days. There are a few instances in which the patient died after the accident with the clinical picture of uremia (Jellinek, Schumacher).

The Blood.—Experiments on hemolysis by electric discharges date back to Rollet and Neumann. Hemoglobinuria after electrocution is

rather common (Chiari, Hackl, Jellinek, Kirmisson, Kawamura, Mott and Schuster, Schmidt, Versé, Wildegans). The extent of the electric burns and the intensity of the hemoglobinuria do not seem to be related. Schmidt found hemoglobin casts in the tubules of the kidney. Hemolytic jaundice, following accidents caused by electricity, was reported by Jaeger and Bazy. Kawamura thinks that the electric shock affects the coagulability of the blood. Alternating currents hasten coagulation, and direct currents delay it. Immediately after the accident, Jellinek found a leukocytosis and the appearance in the peripheral blood of abnormal large white cells.

Other Observations.—In the reports on accidents due to electricity, numerous observations besides those already quoted are given. Many are of little interest and may be omitted. The more important ones may be mentioned briefly. Balkhausen and Grueter found sugar in the urine after exposure to an alternating current from 25,000 volts. Jellinek emphasizes a rise in the pressure of the spinal fluid. He recommends spinal puncture in severe electric shock. Muller found blood in the spinal fluid after an electric stroke from 30,000 volts. The blood was not traumatic in origin. In several cases, especially in electrocuted criminals, an abnormal height of body temperature was recorded. In an immediate death caused by an alternating current of 3,000 volts, Ziemke found that the temperature one hour after the accident was 67 C. in the left axilla, 45 C. in the right axilla and 37.7 C. in the rectum. In an observation of Simonin, an alternating current from 12,000 volts opened the abdominal cavity. There were three perforations in the intestine measuring from 5 to 6 cm. They had ragged edges, and there were hemorrhages in the surrounding area. The patient died thirteen hours after the accident.

CHRONIC DISEASES FOLLOWING ELECTRIC SHOCK

In the majority of cases, the electric shock does not lead to lasting disturbances. The rapidity of complete recovery, even from a severe trauma due to electricity, is often remarkable. When permanent decrease of the earning capacity occurs (according to Natrop, in about 44 per cent of the accidents caused by high tension), it is usually due to the mutilating effect of the electric arc which necessitated the amputation of extremities.

As in other types of accidents, electric currents have been blamed for a large number of functional disturbances. These functional neuroses shall not be discussed here. Moorhead thinks that the nervous symptoms following electric shocks are almost invariably those of the hysteroneurotic type. It seems to me that he goes too far with this statement. There are, no doubt, anatomic nervous lesions which can be considered a result of the accident caused by electricity. Jellinek, in his

book, mentions an ascending peripheral neuritis, causing atrophy of the muscles with sensory and reflex disturbances. Kawamura saw five patients with flaccid paralysis of the extremities among 110 victims of accidents caused by electricity. Natrop described a mononeuritis of the nervus cutaneous femoris lateralis. The prognosis of these pareses is good. Jellinek reports on two observations which suggested lesions in the spinal cord. The lesions developed several weeks after the accident and disappeared completely after a few months.

Crouson, Chavany and Martin devote a paper to persistent choreotic athetotic disturbances following electrocution. There are also observations on change of character, loss of memory, loss of sexual function, etc. (Muller, Jellinek and others).

Jellinek noted a striking rigidity of the peripheral arteries in young workmen employed in electric power plants. Is this rigidity a result of repeated small traumas due to electricity or of the constant exposure to electric fields? In a man, aged 33, Pfalz saw the blood pressure rise to 230 systolic and 155 diastolic a few weeks after an accident due to electricity. It dropped later, but rose again.

DEATH FROM ELECTRIC SHOCK

The mortality of accidents due to electricity is high. Jaeger gives it as 45 per cent. Natrop says that about half of the accidents caused by currents from high tension are fatal. The death rate is 28 per cent in Boruttau's and 23 per cent in Kawamura's material.

The following types of death are distinguished: (1) sudden, instantaneous death at the moment of entrance of the current; (2) delayed death during the passage of the current; (3) interrupted death in which the victim recovers from a short unconsciousness and may be able to free himself, but dies several minutes later—the body may be found some distance from the place of the accident; (4) late death, in which the patient expires suddenly hours or days after the accident; (5) death due to complications, such as severe burns, hemorrhages, infections and embolism (Jellinek, Speed and others). The first two are the most common types (Jellinek, Naville and de Morsier). Type 4 is rare (Jellinek, Balthazard, Zangger, Wyss).

The Mechanism of Death from Electricity.—There is still a controversy as to the ultimate cause of death due to electricity. Disregarding the cases in which the actual destruction of tissues is so extensive as to be incompatible with life, the question now centers about a paralysis of the heart or of the respiratory center.

The first publications on fatal accidents due to electricity suggested that death had been due to an arrest of the heart (Brouardel, 1882; Tatum, 1890; Oliver and Bolam, 1898). This suggestion was not gen-

erally accepted. Shield and Delepine (1885) considered lesions at the base of the brain were essential to cause death. Pla (1891), Buchanan (1892) and Kratter (1894) pointed out that electrocuted persons die from paralysis of the respiratory center. D'Arsonval (1887) spoke of a simultaneous alteration of both heart and respiration.

Cunningham's experiments on dogs seemed to be in favor of those who called death due to electricity cardiac death. Prevost and Battelli showed that the mode of death in animals depended largely on the tension of the current applied. Currents of low tension kill by inducing ventricular fibrillation and currents of high tension do so by causing central paresis of the respiration. Currents of medium tensions (from 400 to 600 volts) have, perhaps, an injurious action on both the heart and the respiratory center (Rodenwaldt and others). Crile and Macleod, Boruttau, MacWilliam and Cluzet and Bounamour also found that electrocuted dogs die from cardiac fibrillation. Urquhart recently reported that when a current of 110 volts passes through the body longitudinally, only 45 per cent of the animals die from cardiac failure. The other animals are killed by a profound paralysis or block of the respiratory, vagus and vasomotor centers. This form of death also occurs when a current enters the brain directly. Urquhart worked on rabbits, and Prevost and Battelli showed that the heart of a rabbit might recover from fibrillation.

Stanton and Krida think that the observations of Prevost and Battelli on dogs also hold true for human beings, namely, that high voltage currents are fatal on account of a central respiratory paralysis and currents of low tension, because they produce ventricular fibrillation. D'Halluin says that bulbar death is most common in accidents with high intensities. The cardiac death is that of low intensities. A similar opinion is expressed by Machlachlan. Naville and de Morsier admit that in a few instances a high voltage current may prove fatal because of respiratory paralysis. In the majority of the cases, however, ventricular twitching leads to death. Jex-Blake believes that primary failure of the heart, undoubtedly, is the most common mode of death. According to Schridde, fibrillation occurs in a few of the cardiac deaths. There is still another unknown form of immediate stopping of the heart.

D'Halluin's method of distinguishing between currents of low and high intensities is better than that of using the voltage for a criterion. In accidents due to high tension, the resistance of the skin usually is high. It amounts to 50,000, 100,000 and more ohms. Thus, more than 5,000 volts will be necessary that an intensity of 100 milliamperes reaches the heart. On the other hand, in accidents due to low tension, the resistance of the skin is markedly lower. In the bath tub, for example, only about 1,200 ohms and 110 volts, perhaps, will have the same effect on the heart as 5,000 volts with a dry skin. The conditions

are entirely different from those in animal experiments when the electrodes are put into the mouth and the rectum—a combination which never will occur in accidents caused by electricity.

Spilsbury, Zimmern and especially Jellinek still adhere to the idea that a paralysis of the respiration causes death in accidents due to electricity. Spilsbury compares the death due to electricity with that following a slight blow against the upper part of the abdomen, an irritation of the nasal or pharyngeal mucosa or an unexpected submersion in cold water. According to him, a sensory stimulation of the nerves of the skin leads to a reflex paresis of the respiratory center. Jellinek and Zimmern support their explanation by the successful resuscitation of electrocuted persons with the aid of artificial respiration. A fibrillating heart never recovers. How is it then possible that so many victims are brought back to life when artificial breathing is continued for a sufficient length of time? It is just the question of resuscitation which makes the problem of such importance.

Postmortem Results.—What does the autopsy of electrocuted persons teach one? Those who believe in death from respiratory paralysis emphasize the observations which are apt to support their view. There is, first of all, the hyperemia and edema of the lungs (Balthazard, Jellinek, Versé). Schridde found a moderate edema of the lungs in 56 per cent of thirty-seven fatal accidents. According to Jellinek, the presence of foamy fluid in the lungs and bronchi speaks against a sudden stopping of the heart, and indicates that the action of the heart has outlasted the respiration. Naville and de Morsier, who favor the cardiac theory of the death due to electricity, try to explain the edema of the lungs on the basis of an initial arterial hypertension. During this hypertension, fluid transudates into the alveoli. When fibrillation starts, the edema has already developed. The mechanism of the edema of the lungs is still undetermined, and many authors consider it an insufficient proof of internal or external suffocation. The same holds true of the second observation, namely, of the subpleural, subepicardial and subpericardial hemorrhages, the so-called Tardieu patches. Finally, the fact that the right part of the heart is filled with dark liquid blood shows only that the victim died suddenly.

The fibrillation of the heart does not leave anatomic lesions. Hence, it cannot be proved on the postmortem table. The cyanotic hyperemia of the abdominal organs described by Naville and de Morsier points, perhaps, to a cardiac failure. Corin cites an observation of the heart which he believes may be important. The left ventricle is much dilated and filled with liquid blood, while the myocardium appears normal. He quotes R. Virchow as saying that this is the picture of an initial paralysis of the heart. In a paralyzed heart, namely, the rigor mortis does not empty the left ventricle, which does not contain blood in death from

respiratory paralysis. Corin's observation so far has been confirmed only by Capogrossi.

In concluding, it may be said that the postmortem observations do not prove any of the theories. This negative statement may stimulate further and most careful studies of the bodies of those killed by electric currents. In the countries in which the autopsy of electrocuted persons is obligatory, the red tape of the coroner's inquest usually delays its performance for at least twenty-four hours. It is then too late to obtain exact information as to the mode of death, because postmortem changes obscure the picture present at the time of the death. The data from electrocuted criminals are not of value, since the condemned persons die under conditions never encountered in accidents due to electricity.

Internal Factors of the Electric Death.—Several inherent factors, to a certain degree, apparently determine the death or the survival following an accident caused by electricity. One may distinguish constitutional and conditional factors. Regarding the constitution, little attention so far has been given to differences in the race. In Japan, however, fatal accidents caused by electricity are no more or less common than in Europe. A survey of the distribution among the white and colored population of the deaths due to electricity in the United States would be interesting. Most of the victims are men. This, no doubt, is due to the much greater chances of men than of women to receive electric shocks. Age, apparently, does not play a rôle (Jellinek), although some of the experimental workers believe that young animals are less easily killed by electric currents than old ones.

Several investigators emphasize the importance of the status thymicolymphaticus. In Schridde's cases, almost all the victims of accidents caused by electricity showed a hypoplastic constitution. They were long and slender persons with short necks and long legs. The skin was pale and tender and the hair growth around the sex organs was heterosexual or intersexual. The thymus was large. Its weight amounted to as much as 78 Gm. Marked hyperplasia of the medulla was seen. The lymphatic tissue throughout the body was well developed. The significance of the status thymicolymphaticus also was pointed out by Boruttau, Neureiter and Versé. Strassman thinks it is no more common in fatal accidents due to electricity than in other sudden deaths. Since more is known about the normal human thymus, the status thymicolymphaticus has lost much of its importance. Many authors now feel that it should be done away with.

Of the conditional factors, the anticipation of the shock (Jellinek's Strombereitschaft) is most interesting. Aware of the danger, one may stand an electric shock which would be fatal if the current entered the body unexpectedly (Jellinek, d'Arsonval). In the literature, a case is

often quoted of a man who used to demonstrate the passage of a direct current of 500 volts through his body. The man was killed by the same current when he once accidentally touched the live wire. The expectation of the stroke, perhaps, is also the reason why persons who attempt suicide by means of electric current often survive.

Some observations indicate that the resistance against electric currents is increased during sleep (Jellinek, Aspinal). Even Seneca made the statement that sleep protects against death from lightning. The effect of anesthesia is not yet definitely determined. Jellinek thinks that anesthesia protects, while Weiss and Jacon did not find any effect.

A considerable number of persons killed by electric currents reveal preexistent anatomic lesions on the postmortem table. This holds true especially for the accidents due to currents of low tension. Balthazard, Fuerth, Meixner, Neureiter, Ziemke and Fagnet described changes of the heart such as hypertrophy and dilatation, myocardial degeneration and valvular changes. On the other hand, Jellinek found that people with diseases of the heart could stand even severe electric shocks. Luther believes that alcoholism and exophthalmic goiter are predisposing to death due to electricity. Frommolt saw an acute catarrhal enteritis in a boy who died from an electric shock. Neureiter goes so far as to say that many of the deaths due to electricty can be explained by preexistent pathologic changes, without the action of the current. In some of his and Meixner's cases, however, the evidences quoted to support his opinion are not convincing. Thus, he speaks of an acute glomerulonephritis without microscopic proof.

RESUSCITATION FROM ELECTRIC SHOCK

The most important method of resuscitation is artificial breathing (d'Arsonval, Jellinek, Jex-Blake, Zimmern and others). The prone pressure method, after Schaefer, is most commonly used in the United States and Canada, and has been accepted generally (Drinker, Maclachan, Urquhart and others). In order to obtain good results, artificial respiration should be started as soon as possible and continued for a sufficient time, even for hours. Indeed, nothing should stop it except such signs of cessation of life as cooling of the body, formation of livid patches and onset of rigor mortis.

The artificial respiration makes possible the resuscitation of the paralyzed respiratory center. What can be done to overcome the cessation of the circulation? The passive movements of the chest also will produce a slight circulation which, together with the ventilation of the blood, is often sufficient to revive the vital centers. They do not have any effect on the heart itself, when it is fibrillating. Prevost and Battelli succeeded in restoring normal rhythmic contractions of fibrillating hearts by a shock of high voltage. D'Halluin says that a

fibrillating heart can be revived by currents of high tension within fifteen seconds after it has started twitching. Haberland considers the possibility of making practical use of this method in fatal accidents. It is doubtful whether it will ever be possible to carry out his suggestion. The time limit is too short for making all the necessary preparations. There are only a few places where the currents required are always at hand, provided one would take a chance of exposing the body of a lifeless individual to an electric shock of several thousand volts.

Direct massage of the heart and intracardial injection of salt solution free from calcium and containing camphor were recommended by Boruttau. Massage of the heart is not of value according to Kroneker, Battelli and Hering. D'Halluin obtained some promising results in experiments on animals with the intravenous injection of potassium chloride. Experiments also have shown that ventricular fibrillation disappears when the blood pressure in the coronary arteries is increased. Stanton and Krida base some therapeutic speculations on these observations.

In order to complete this list, the so-called counter shock may be mentioned. The counter shock has the following underlying observation. Apparently, victims of accidents caused by electricity are more likely to start breathing spontaneously, if they fall from some height after receiving the shock. An attempt was made to make use of this theory in several methods of resuscitation, but none were of any value (Campbell and Hill, Urquhart).

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Notes and News

University News, Promotions, Resignations and Appointments.—George T. Pack, professor of pathology in the University of Alabama has accepted an appointment in the Memorial Hospital for Malignant Diseases, New York, and will take up his new duties on July 1, 1928.

Stewart Graves, professor of pathology since 1914 and dean of the School of Medicine of the University of Louisville, has accepted an appointment as professor of pathology and dean of the School of Medicine of the University of Alabama.

It is reported that Henry C. Hartman has resigned as professor of pathology and dean of the School of Medicine of the University of Texas at Galveston.

Ernest Ruckensteiner has resigned his instructorship in pathology in the school of medicine of Creighton University, Omaha, and has returned to Vienna.

Aristides Agramonte, of Havana, a member of the United States yellow fever commission consisting of Reed, Carroll, Lazear and Agramonte, has been awarded the degree of Doctor of Laws by Tulane University, New Orleans.

Georg B. Gruber, Innsbruck, has been appointed professor of pathology at Göttingen in the place of Eduard Kaufmann retired.

J. H. J. Upham has been appointed dean of the College of Medicine of Ohio State University.

Charles W. Young has been appointed associate in comparative pathology in the Harvard Medical School.

At the University of Pittsburgh, H. L. Menten and Mortimer Cohen have been promoted to associate professors of pathology, and Andrew Wallhauser has been appointed assistant professor of bacteriology and pathology.

H. G. Little has been appointed pathologist at the William H. Singer Memorial Research Laboratory in Pittsburgh.

Garner Scullard has resigned as pathologist at the Ohio Valley General Hospital, Wheeling, W. Va., to become pathologist to the South Side Hospital in Pittsburgh.

Martin H. Lovel has been appointed assistant in pathology at Meharry Medical College, Nashville, Tenn., and resident pathologist to the George W. Hubbard Hospital, succeeding J. Reginald Cuff.

David R. Morgan has been appointed curator of the museum and demonstrator of pathology in the Jefferson Medical College, Philadelphia.

Department of Embryology, Carnegie Institution of Washington.—This department maintains a diagnostic service for physicians and is under the charge of C. H. Heuser. Each year about 600 embryologic specimens are received for examination and diagnosis. Expert opinions are given on such questions as age, sex, race, anomalous development, pathologic conditions and, in some degree also, on the cause of the abortion. The address is Wolfe and Madison Streets, Baltimore, Md.

Lane Lectures.—The Lane Lectures of the School of Medicine of Stanford University will be given by F. d'Herelle, Alexandria, Egypt, during the week beginning with October 22 next. The subjects will be bacteriophagy, bacterial mutation, infectious diseases, the phenomenon of recovery, and logic in biologic research.

Lasker Foundation.—The Lasker Foundation for Medical Research has been established at the University of Chicago with an initial endowment of $1,000,000, by Albert D. Lasker and Flora W. Lasker. Research under the spirit of the endowment is to be directed toward establishing the causes, nature, prevention and cure of so-called degenerative diseases (Bright's disease, heart disease, etc.).

Abstracts from Current Literature

Pathologic Physiology

THE SIGNIFICANCE OF THE PERICARDIUM IN ACUTE CARDIAC DILATATION PRODUCED BY ANOXEMIA. E. J. VAN LIERE and R. S. ALLEN, Am. J. Physiol. **83**:225, 1927.

Severe anoxemia was found to produce greater cardiac dilatation in animals — cats, dogs and especially monkeys — in which the pericardium had been removed. The writers believe that the restraining action of the pericardium seldom comes into play in the normal animal — only in cases of extreme cardiac stress.

H. E. EGGERS.

STUDIES ON THE ANEMIA OF RICE DISEASE IN PIGEONS. O. W. BARLOW, Am. J. Physiol. **83**:237, 1927.

The depressive effects of rice disease on the body weight, respiration, temperature and red cell count of pigeons, which parallel those of partial starvation, were not prevented by the administration of loosely bound hydrochloric acid (betaine HCl), or butter and orange juice. The anemia was prevented by the administration of lactose, mineral oil or magnesium sulphate, without influencing the other depressive effects. It is suggested that this effect is due to the action of these substances on the intestinal flora, with consequent diminution of the bacteremia.

H. E. EGGERS.

THE INFLUENCE OF THE THYROID GLAND ON THE PRODUCTION AND CONTROL OF EXPERIMENTAL RICKETS. M. M. KUNDE and L. A. WILLIAMS, Am. J. Physiol. **83**:245, 1927.

In cretin rats the addition of cod liver oil to a ricket-producing diet, and to a diet nutritious and rich in vitamins, was without effect in both instances in preventing the development of that disease, as indicated by histologic changes in the epiphyses.

H. E. EGGERS.

THE EFFECTS OF ANOXEMIA OF MILD DEGREE ON THE CARDIAC OUTPUT OF UNNARCOTIZED DOGS. T. R. HARRISON, C. P. WILSON, D. NEIGHBORS and C. PILCHER, Am. J. Physiol. **83**:275, 1927.

As a result of the study of the cardiac output of normal, unanesthetized dogs by means of the Fick method, it was found that the breathing of oxygen did not affect the minute output; with the arterial blood less than 70 per cent saturated with oxygen, the minute output was increased; with saturations of 80 per cent and over, the minute output was usually unchanged. Since the first changes were usually observed with a saturation of 75 per cent, the writers term this the "anoxemic threshold." In anoxemia there was a slight increase in pulse rate and a great increase in minute ventilation and respiratory quotient. Only in extreme degrees did there occur any great alteration in the rate of oxygen consumption.

H. E. EGGERS.

THE BASAL METABOLISM IN PULMONARY TUBERCULOSIS. BENJAMIN L. BROCK and CHARLES H. HASKINS, Am. Rev. Tuberc. **16**:83, 1927.

The basal metabolism of tuberculous patients may be normal or below the average normal. In five patients studied the rate varied between approximately minus 19 per cent and minus 3 per cent of the average normal (DuBois standards). A comparison of the average basal metabolisms of two tuberculous patients studied both in winter and in summer, according to the regular routine,

showed a decrease of 9 per cent and 13.2 per cent in summer as compared to winter. This was believed to be due to the long period of inactivity rather than to any environmental change. Undernourishment may account for low metabolism, as compared to the normal, as well as inactivity. Exposure of tuberculous patients to atmospheric conditions prevailing in winter, causes an immediate temporary rise in the metabolism rate with a subsequent fall. In summer, treatment outdoors under basal conditions causes a gradual rise in the rate even though the temperature of the room is lower than that outside. In winter the powers of the person to adapt himself to the conditions of the environment are called on to a greater extent than in summer. Although it is not definitely proved it seems that no extra work is thrown on the lung of patients with tuberculosis treated outdoors in winter or summer, and that the mild stimulation they receive from this treatment may be of definite benefit.

H. J. Corper.

The Problem of the Iron Reserve: An Experimental Study. Charles Spencer Williamson and Harold N. Ets, Arch. Int. Med. **40**:668, 1927.

A reservoir of readily utilizable iron can be built up in the livers and spleens of rats by placing them on a diet containing liver. This stored iron can be used in the regeneration of hemoglobin after the production of anemia by bleeding. Rats rendered anemic by bleeding, the iron reserve of which has been exhausted, recover their concentration of hemoglobin rapidly on being placed on a diet containing liver, and simultaneously build up a reserve of iron in the livers and spleens.

Authors' Summary.

Effect of Pregnancy on the Emptying of the Gallbladder. F. C. Mann and G. M. Higgins, Arch. Surg. **15**:552, 1927.

The authors found that in the dog, guinea-pig and gopher, pregnancy delays the emptying of the gallbladder in response to a meal of cream and egg yolk. By using paraffin balls they were able to show that the mere increase in the abdominal contents did not delay the emptying time of the gallbladder. The interpretation of the influence of pregnancy on the gallbladder must await further information concerning the normal mechanism of the gallbladder.

N. Enzer.

Changes in the Chemistry of the Contents of the Stomach Following Gastric Operations. M. E. Steinberg, J. C. Brougher and I. J. Vidgoff. Arch. Surg. **15**:749, 1927.

After a gastro-enterostomy is performed, the acidity of the gastric juice is unaltered, but the amount of gastric secretion is reduced. The fundus will secrete gastric juice of high acidity when various substances are introduced into it, after the antrum has been separated from it. If the antrum is removed, the free acidity of the stomach contents is reduced or absent. This is due largely to neutralization of the gastric secretion by the influx of alkaline secretion from the intestines.

N. Enzer.

The Relation of the Suprarenal Gland and the Spleen to Cholesterol Metabolism. F. S. Randles and A. Knudson, J. Biol. Chem. **76**:89, 1928.

Removal of the spleen or of the suprarenal glands does not have any apparent effect on the blood cholesterol concentration in the rat.

Arthur Locke.

Vitamin A Deficiency and Urolithiasis. E. C. van Leersum, J. Biol. Chem. **76**:137, 1928.

Vitamin A deficiency may be the cause for the occurrence of phosphate calculi in the urinary tracts of rats. The kidneys, bladder and urinary tracts of 886 rats were examined for the presence of calculi. Calculi were not found in 241 normal

controls. Among the remaining 645 rats, all of which had been maintained on a diet deficient of vitamin A, calculosis was found in 130 of the males and in sixty-seven of the females. It is suggested that the deposition of calcium casts may have been the result of a keratinization of the epithelial cells of the tubules consequent to the deficiency of vitamin A.

ARTHUR LOCKE.

THE EFFECT OF OVERBREATHING AND OF BREATHING RELATIVELY HIGH CONCENTRATIONS OF CARBON DIOXIDE ON THE URINARY EXCRETION OF WATER AND CHLORIDES. G. E. SIMPSON and A. H. WELLS, J. Biol. Chem. **76**:171, 1928.

The quantity of water and of chloride excreted in the urine may be inversely proportional to the alveolar carbon dioxide tension. It is increased on waking from sleep and during forced breathing and is decreased in an atmosphere with a high concentration of carbon dioxide.

ARTHUR LOCKE.

EFFECT OF CERTAIN TISSUE EXTRACTS ON RED BLOOD CELL REGENERATION IN THE RABBIT. ANDREW JENEY and JAMES W. JOBBLING, J. Exper. Med. **46**:839, 1927.

Extracts of liver, as a rule, did not cause as active regeneration of red cells in rabbits as they apparently do in the dog.

THE ACTIVITY OF THE THYROID GLAND IN RELATION TO THE STAINING REACTIONS OF THE COLLOID. EVELYN E. HEWER, J. Path. & Bact. **30**:621, 1927.

It is possible to gage the degree of activity of the stored thyroid secretion by the staining reactions of the colloid. Freshly secreted active material gives an alkaline staining reaction, whereas the old or inactive material is acid. The activity of a portion of gland removed at operation is not always directly related to the basal metabolic rate. The staining variations depend on the acid-alkaline reaction of the colloid, and not on its iodine content.

AUTHOR'S SUMMARY.

METABOLISM IN MANIC AND DEPRESSIVE CONDITIONS. E. KLEMPERER, Jahrb. f. Psychiat. u. Neurol. **45**:32, 1927.

In simple melancholia the calcium content of the blood was decreased and the potassium was normal; in anxiety melancholia the calcium was increased and potassium normal. Stuporous melancholic persons had an increased calcium and a decreased potassium content. In catatonic stupor with marked muscular rigidity the calcium content was increased. Manic patients showed a normal calcium content.

ROY GRINKER.

ACTION OF INSULIN AND OF HYPOGLYCEMIA ON THE HUMAN HEART. HARRY SCHÄFFER, ELSA BUCKA and KURT FRIEDLÄNDER, Ztschr. f. d. ges. exper. Med. **57**:35, 1927.

The influence of large doses of insulin has been followed on the healthy and the diseased human heart in diabetic and nondiabetic patients by means of the electrocardiogram. In the first group of experiments the studies were made under conditions of fasting, so that a hypoglycemia was produced. In the second group, the blood sugar content was maintained at normal or supernormal levels by means of a copious carbohydrate intake.

Disturbances of cardiac function were observed on the clinically healthy and, in a more marked degree, on the diseased hearts. Diabetic and nondiabetic patients did not show any estimable difference. The disturbances were: increase in pulse rate (in a few cases decrease); the previously observed flattening of the T wave (which often was preceded by an increase in size); changes in the form of the P wave; lengthening of the ventricular complex

(Q T), and sometimes also of the Q R S interval; conduction disturbances with occasional omission of ventricular systole and pulsus alternans, and, especially, frequently various forms of extrasystolic arrhythmia.

Some of these changes, such as the increased rate and the change in form of the T wave, were found to be independent of the blood sugar level and must be explained as direct insulin action on the heart muscle.

On the other hand, the slowing of the Q R S interval, the change in form of the P wave, occasionally observed bradycardia, alternation and loss of the ventricular systole and the extrasystoles were observed only during the hypoglycemia and, therefore, are to be considered as results of hypoglycemia and not due to the insulin directly.

In every case of hypoglycemia there is the danger of a functional disturbance of the heart. Its avoidance, therefore, in all forms of treatment with insulin must be carefully observed.

BALDUIN LUCKE.

RÔLE OF SPLEEN IN BLOOD FORMATION. S. WEISS and E. KOLTA, Ztschr. f. d. ges. exper. Med. **57**:157, 1927.

After roentgen-ray treatment of the spleen of dogs a decrease occurred in the number of leukocytes in the peripheral blood, while the number of erythrocytes increased. Watery and alcoholic extracts of the spleen of dogs subjected to treatment with roentgen rays and injected into rabbits caused a marked increase in the number of erythrocytes; the white cells remained unchanged. Extracts of spleen not previously treated with the roentgen ray did not produce any change in the number of leukocytes or erythrocytes.

BALDUIN LUCKE.

Pathologic Anatomy

ECHINOCOCCUS CYST OF THE ORBIT IN A CHINESE. HARVEY J. HOWARD, Am. J. Ophth. **10**:727, 1927.

The case of a Chinese farmer, aged 42, who had a large mass of three years' duration protruding from the left orbit, is reported as the first echinococcus cyst of the orbit reported from China. Diagnosis was made by aspirating fluid which contained hooklets and scolices. Complete exenteration of the orbit was performed. The pathologic report showed a unilocular cyst, with double chitinous wall, to which were attached daughter and grand-daughter cysts. No vestige of echinococcus was found within the eyeball. The only pathologic effect on the eye was due to pressure from behind. Three per cent eosinophils were present in the blood, and a local eosinophilia was also evidenced.

BENJAMIN RONES.

TUBERCULOUS STRICTURE OF THE OESOPHAGUS. REPORT OF A CASE. PORTER P. VINSON and HERBERT E. DOBSON, Am. Rev. Tuberc. **16**:53, 1927.

The rarity of tuberculous infection of the esophagus is pointed out and an interesting case reported in a merchant, aged 46, which presented special features from the standpoint of diagnosis and management. The stricture was dilated by means of a sound and histologic examination of the tissue removed proved the presence of tuberculosis.

H. J. CORPER.

CEREBRAL TUBERCULOSIS IN ADULTS: CASE REPORTS. B. M. RANDOLPH and THOMAS CAJIGAS, Am. Rev. Tuberc. **16**:57, 1927.

Nine cases are reported which presented certain interesting points. In all the cases of acute cerebral tuberculosis there was a blood leukocytosis with a high polymorphonuclear percentage. Tubercle bacilli were not found in direct smears from the spinal fluid in only two of the cases, and in these only a single spinal puncture was made. In the others, it was found at the first or second tapping.

As the outcome is invariably fatal, the only practical value of a diagnosis before death is to establish the prognosis and to save the patient futile and trying therapeutic procedures. In cases in which the diagnosis is not made from examination of the spinal fluid, guinea-pig inoculation ultimately settles the question, but, as a rule, this result is not obtained until after death. The cell count was increased in all cases, pleocytosis usually being more marked as the disease progressed. The relative percentage of polymorphonuclears varies. The lymphocytes are usually in excess, sometimes two to one, but in some cases this figure is reversed, the polymorphonuclears predominating. The globulin content was consistently high, more or less rising with the cell count. The clinical picture of tuberculous meningitis is extremely variable. It is the author's belief that except in those cases in which the meningitis is a terminal phenomenon in generalized tuberculosis, it arises from a cerebral focus already present. Autopsy in these cases does not usually reveal any evidence of unhealed or recent tuberculosis elsewhere in the body, and the clinical history supports the hypothesis that the meningitis arises from a cerebral focus. Autopsy on these subjects often reveals one large tubercle in the substance of the brain, from the size and structure of which it is apparent that possibly it has existed for several months. The meningeal involvement is always by young tubercles of the miliary type, widely diffuse throughout the leptomeninges and with accumulation of fibrin at the base of the brain and this process was distinctly one of rather short duration.

H. J. Corper.

The Origin and Dissemination of Tuberculosis According to Recent Investigations. F. Neufeld, Am. Rev. Tuberc. **16**:66, 1927.

This is a review article and not suitable for abstracting.

H. J. Corper.

Multiple Myeloma, with Report of a Case. Thomas J. Charlton, Arch. Int. Med. **40**:98, 1927.

A case report is given of multiple myeloma occurring in a woman, the patient being under observation for over two and one-half years. Attention was first directed to the condition by a pain in the back, made worse by pressure. Bence-Jones protein was found in the urine, and on the basis of these two conditions a provisional diagnosis of multiple myeloma was made; roentgen-ray observations confirmed the diagnosis. The blood picture was that of marked secondary anemia. The icteric index and hemosiderosis of the liver and spleen at autopsy suggested that the anemia, to a certain extent, may have been of a hemolytic nature. The course of the disease was marked by progressive anemia and many pathologic fractures. At autopsy, several pathologic fractures were seen, and most of the bones were destroyed by the tumor growth of the marrow. The histologic structure of the tumor tissue was that of a plasmocytoma. No metastases were found, but plasma cells were present in the capillaries of the liver.

Author's Summary.

Normal Variations in White Blood Cells Under Conditions of Minimal Metabolism. R. P. Stetson, Arch. Int. Med. **40**:488, 1927.

The polymorphonuclear neutrophils were fewer and the lymphocytes more numerous than usual during the day. The average percentage of the former was 51.04 and of the latter, 36.04. Daily variations in the white blood cell count were beyond the limits dependent on technical or mathematical errors. Each type of cell shared in the fluctuations. The average percentage of polymorphonuclear neutrophils and lymphocytes maintained different levels during different periods of the year. Immature cells of both myeloid and lymphoid origin were encountered rarely.

Author's Summary.

POSTOPERATIVE LUNG ABSCESS: AN EXPERIMENTAL STUDY. S. A. SCHUETER and I. F. WEIDLEIN, Arch. Surg. **14**:457, 1927.

Failure to produce lung abscess by the introduction of foreign material into the trachea led to the theory that abscess is most frequently the result of septic emboli, and the authors were successful in producing abscesses in the lung by freeing septic emboli into the circulation. The intrabronchial injection of various foreign bodies and cultures of organisms failed to produce a single lung abscess in fifteen dogs. A method of introducing septic emboli into the jugular vein is described. When cultures containing two or more organisms were used, the results were more satisfactory. *Staphylococcus aureus, Bacillus coli,* pneumococcus and streptococcus gave the best results. The suppuration which resulted never became chronic but showed evidences of healing in thirty-three days. This is probably due to the fact that the natural horizontal position of the dog facilitates drainage. Unless the embolus is enclosed in a capsule, localization will not occur and a suppurative pneumonitis results. The abscess is apparent within from eighteen to twenty-four hours after the embolus is lodged and in from three to four days the surrounding lung tissue is widely inflamed. As the abscess increases in size a surrounding fibrous wall is developed, and healing takes place after evacuation of the abscess with scar tissue formation. The abscess will encroach on and destroy moderately sized bronchi. These experiments deal only with parenchymatous abscesses and not those of the bronchiectatic variety. They tend to prove that postoperative lung abscesses are embolic in origin, and the authors support their experimental evidence by clinical facts, such as the occurrence of lung abscess after local anesthesia in abdominal operations, and the high percentage following operation in mobile areas.

N. ENZER.

ISOLATED GIANT CELL XANTHOMATIC TUMORS OF THE FINGERS AND HAND. M. L. MASON and W. H. WOOLSTON, Arch. Surg. **15**:499, 1927.

These tumors are characterized by the presence of foam cells and foreign body giant cells. The etiology is obscure, but trauma is to be considered of some significance. They occur more frequently in adults. Determination of the amount of cholesterol in a few of the cases did not show an increase in the blood cholesterol. In this respect, these tumors differ from the xanthoma multiplex. They may take origin from the tendon sheaths or subcutaneous and other fibrous tissue. They vary in size and are generally a yellowish red. Their consistency is firm. The capsule sends trabeculae into the tumor, dividing it into irregular lobules.

Microscopically, the presence of the foam cells and foreign body giant cells is characteristic and most frequent; yet one or the other may be absent. Other cells are present, chiefly proliferating fibroblasts and reticulo-endothelial cells. The foam cells are large, polyhedral and filled with lipoid. The giant cells are of the foreign body type and frequently filled with pigment. The tumors are fairly vascular and generally permeated by sinuses. These tumors are benign. They are among the most common tumors of the fingers, and their growth is usually slow. Several have recurred locally.

N. ENZER.

THE PATHOGENESIS OF BLADDER DIVERTICULA. D. K. ROSE, Arch. Surg. **14**:554, 1927.

The author believes that there must be a congenital defect in the form of a loose intramural fibrous pathway before raised intracystic pressure can herniate the mucosa. Therefore, unless the intracystic pressure of the fluid used in cystoscopy is known and controlled, small balloonings may be produced in

areas that are potentially diverticula. These are sufficiently elastic to disappear with removal of the pressure and only remain as diverticula with prolonged destruction or infection.

N. Enzer.

Syphilitic Ulcerations of the Stomach. B. Kwartin and C. G. Heyd, Arch. Surg. **14**:566, 1927.

The authors describe the gross and microscopic appearances in three ulcers of the stomach which clinically and grossly were quite distinct from the classic peptic ulcer. One they concluded was syphilitic, one tuberculous and one nonspecific. They stress the difficulty of making a differential diagnosis between syphilis and tuberculosis and place the ultimate criterion in the finding of the spirochete or tubercle bacillus.

N. Enzer.

Extra-Renal Venous Circulation in a Case of Congenital Polycystic Kidneys: An Unusual Varicocele Communicating Between the Splenic and Renal Veins. E. Duskes, Arch. Surg. **15**:580, 1927.

This lesion is explained as being an abnormal development of a normal communicating venule between the capsular and splenic venules.

N. Enzer.

The Bilaterality of the Liver. A. H. McIndoe and V. S. Counseller, Arch. Surg. **15**:589, 1927.

By methods of injection, it is shown that the liver is divided into a right and left lobe, each of which is drained by a branch of the bile duct and supplied by a branch of the portal vein and hepatic artery. Intercellular sinusoids, insufficient to establish a collateral circulation, exist between the two divisions of the portal vein. To a lesser extent, the two divisions of the hepatic artery communicate chiefly through capsular branches. The latter are not sufficient to prevent infarction. There is no communication between the two biliary divisions; hence the falciform ligament is not a true anatomic landmark, which is more nearly placed by a line from the fossa of the gallbladder to the entrance of the hepatic vein into the inferior vena cava.

N. Enzer.

Spontaneous Gangrene of the Extremities. Dean Lewis, Arch. Surg. **15**: 613, 1927.

This study is based on a series of 137 cases of gangrene due to arteriosclerosis, arteriosclerosis and diabetes, diabetes without prominent vascular lesions, thrombo-angiitis obliterans, scleroderma and infection. It is of particular interest because of the roentgen-ray photography of amputated extremities in which the arteries were injected with an opaque substance. The development of collateral circulation in thrombo-angiitis obliterans is striking.

N. Enzer.

Suprarenal Hemorrhage. C. E. Farr and K. Semsroth, Arch. Surg. **15**:627, 1927.

This is a case report of massive hemorrhage from the suprarenal gland in a man, aged 34. The condition was not diagnosed before exploratory operation.

N. Enzer.

Cysts of the Semilunar Cartilages of the Knee. I. Zadek and H. L. Jaffe, Arch. Surg. **15**:677, 1927.

The case reported here is the third in the literature of cysts of the internal cartilage. The authors regard these as true cysts, probably congenital in origin. The cysts were lined by a synovia-like endothelium.

N. Enzer.

ACUTE TRAUMATIC ULCERS OF THE SMALL INTESTINES: OBSERVATIONS ON THE EFFECTS OF APPLICATION OF CLAMPS ON THE GASTRO-INTESTINAL TRACT. W. J. GALLAGHER, Arch. Surg. **15**:689, 1927.

The effects of pressure on various portions of the intestinal wall was studied by a method which permitted the pressure applied by the clamps to be measured in millimeters of mercury. When the pressure was sufficient to produce local anemia, ulcers resulted after the clamps had been applied for thirty minutes. Thus typical acute ulcers of the duodenum resulted, the area and extent of the ulceration varying with the duration of the pressure. The ulcers heal and scar. If the nutrition of the animal was impaired by ligation of the pancreatic duct, delay in healing resulted; otherwise, these ulcers healed rapidly. The large bowel and gastric mucosa were found to be resistant to trauma from clamps. It is possible that trauma produced by clamps may be a contributing factor in the genesis of some forms of chronic experimental ulcer in dogs.

N. ENZER.

FATE OF FOREIGN BODIES IN VENOUS CIRCULATION. H. J. WARTHEN, JR., Arch. Surg. **15**:712, 1927.

In fourteen dogs, ninety-four metallic foreign bodies were introduced into the circulation by way of the femoral and jugular veins. Sixty-seven of these reached the heart, but only three were found in the heart at autopsy. The remaining sixty-four lodged in the lungs. They caused infarcts which apparently gave rise to little disturbance in the pulmonary circulation. The three objects that lodged in the heart were found near the apex of the right ventricle.

N. ENZER.

THE QUANTITATIVE BIOLOGICAL EFFECTS OF X-RAYS OF DIFFERENT WAVE-LENGTH. CHARLES PACKARD, J. Cancer Research **11**:1, 1927.

It is accepted that both hard and soft rays produce the same kind of morphologic changes in living cells. It remains, however, to elucidate whether the amount of such changes varies with the quality of the beam. The results obtained by different workers vary because of the difficulty in measuring the intensity of the beam and the extent of biologic change produced in the cell. Packard gives in detail the roentgen-ray technic used by him. The experiments were conducted on the eggs of the fruit fly, *Drosophilia*. The use of the eggs of *Drosophilia*, permits thousands of specimens to be irradiated at once, and thus one can avoid the error of drawing conclusions based on the behavior of a few highly variable objects. Then again, each individual is uniformly radiated throughout. From the author's experiments, it appears that when the intensity and duration by exposure are equal, these two beams of widely different qualities, the one composed chiefly of hard rays and the other of both hard and soft, have the same lethal effect on the eggs of *Drosophilia*. His conclusions are that homogeneous roentgen-ray beams of equal intensity, but of different wave-length produce the same quantitative biologic effects on *Drosophilia* eggs. The same holds true for heterogeneous beams of equal intensity. Ionization measurements and biologic effects are parallel within the range of wave length tested.

B. M. FRIED.

THE OCCURRENCE OF BRAIN TISSUE WITHIN THE NOSE. D. GUTHRIE and N. DOTT, J. Laryng. & Otol. **42**:733, 1927.

A man, aged 33, died thirteen days after a left subtemporal decompression operation for the relief of coma induced by a glioma of the left frontal lobe. The brain was fixed in 10 per cent formaldehyde in situ and subsequent examination disclosed an extension of the glioma into the left nasal cavity with an early pyogenic infection. The explanation for the nasal growth hinges on the

well known fact that increased intracranial pressure leads to herniation of the brain through the natural minute aperatures as the openings for the arachnoidal villi. Added to this are the proliferating and infiltrating activities of a neoplasm in the region of the crista galli where such openings are particularly numerous.

Another man, aged 46, had been struck on the head with a wooden beam, bled profusely from the nose and shortly afterward developed a gradual paralysis of the right arm and leg. He had coma at intervals for fifteen years and on two occasions had polypi removed from the left nasal cavity but histologic study was not made. In the authors' case a pigeon-egg sized left nasal polyp containing 1 drachm of straw-colored fluid was removed, but the exact origin of the pedicle was not determined. Histologic sections revealed three layers in the polyp: a ciliated epithelial covering, and edematous submucosa unfiltrated with small branching connective tissue cells and a central part containing glia cells. The authors think the glia tissue was in the nose since birth and then became incorporated in a nasal polyp, hence this tumor should be called an "encephalocele" rather than a nasal glioma.

GEORGE RUKSTINAT.

NOTE ON SOME PATHOLOGICAL CHANGES IN THE TISSUES DURING ATTEMPTED ACCLIMATIZATION TO ALTERATIONS OF OXYGEN PRESSURE IN THE AIR. J. ARGYLL CAMPBELL, Brit. J. Exper. Path. **8**:347, 1927.

Cats, monkeys, rabbits, cavies, rats and mice were exposed to various pressures of oxygen in the air ranging from a maximum of 200 per cent above normal to a mininum of 60 per cent below normal.

Prolonged exposure to low oxygen pressures resulted in symptoms suggesting heart failure. Postmortem examination revealed a general state of vascular congestion and fatty degeneration of the heart, the latter being most marked in cavies. In cats, the tunica muscularis of the pulmonary vessels, particularly the arteries, was hypertrophied.

High oxygen pressures noticeably affected only the cats, causing weakness and loss of weight. Histologically, there was general wasting of tissues and collapse and congestion of some of the alveoli of the lung. There was no evidence of a true pneumonia. These effects possibly are due to a toxic action of oxygen on the epithelium of the lung.

S. D. SIMON.

PIGMENTED AND PURPURIC DERMATITIS OF THE LEGS, A CONTRIBUTION TO THE STUDY OF A CLINICAL VARIETY OF A HEMORRHAGIC SYPHILIS OF THE LOWER EXTREMITIES. M. FAVRE and A. CHAIX, Ann. de méd. **22**:45, 1927.

The lesion described is commonly designated as varicose eczema, varicose pigmentation or varicose ulcers of the legs. It is of frequent occurrence and affects the legs above the maleoli, being conspicuous as brown spots accompanied by changes in the veins and complicated by persistent cutaneous ulcers.

From an investigation of sixty cases, the conclusion is reached that patients with this disease show frequently important organic lesions elsewhere in the body: aortitis, hypertension and cardiac arrhythmias. In brief, the patients are "polysclerotic." Although the authors designate the disease as "a variety of a hemorrhagic syphilis," the histology of the lesion as given by them is not characteristic of syphilis. Moreover, only thirty-five of the sixty-six patients gave a positive Wassermann reaction.

B. M. FRIED.

CONCERNING THE MYELO-NEURO-MYOPATIC FORM OF KUSSMAUL'S DISEASE. G. MARINESCO and S. DRAGANESCO, Ann. de méd. **22**:154, 1927.

The case of periarteritis nodosa reported by Marinesco and Draganesco concerned a man, aged 39, with a definite history of syphilis of eight years' duration. On admission to the hospital, the patient showed a high temperature,

loss of weight, symptoms of the gastro-intestinal tract, albuminuria, secondary anemia and a polyneuritis. He died six months after admission. Under the microscope the most outstanding lesion was found in the arteries which the authors identify as endo-meso-periarteritis in the stage of cicatrization. In a previous case which the authors have investigated, they have distinguished three stages in the vascular lesion: the initial stage with swelling of the endothelium and a polymorphonuclear leukocytic infiltration of the adventitia; the second stage which is dominated by infiltration with lymphoid and plasma cells and by a homogeneous media, and finally, the third stage which is characterized by a fibroblastic invasion leading to a transformation of the vessel into a cordlike structure. The case reported corresponds to the third stage of the disease. Besides the vessels, degenerative lesions are found in all the viscera. In the heart the lesion is more pronounced in the branches of the coronary arteries. In the nerves and the spinal ganglia, and in the nerve roots, there are advanced degenerative lesions. In the spinal cord, there is a scattered lymphocytic infiltration. Of particular interest are the small neuroglia nodules in the anteriolateral horns of the white substance. These resemble closely those found in typhus fever.

Marinesco and Draganesco designate the disease as Kussmaul's malady, who was first to give a clear description of periarteritis nodosa. They consider the disease as an autonomous entity. It is probably caused by an ultravirus which has a mesodermal predilection spreading by way of the vaso vasorum. It has nothing in common with syphilis.

B. M. Fried.

Polyneuritis Due to Anemia. Ludo Van Bogaert, Ann. de méd. **22**:321, 1927.

From a review of the literature, Bogaert concludes that neuritic lesions due to anemia are more frequent than one believes. In one of six cases with neuro-anemic symptoms, which he studied, the patient suffered with a typical polyneuritis. The histology of the lesion was that of a parenchymatous degeneration when the pathologic changes of the myelin sheath and axis cylinders developed parallel to reactions of the neurolemma. The disease is a clinical as well as a pathologic entity.

B. M. Fried.

Contribution to the Histophysiology of the Pleura and Reactions of the Pleura of the Guinea-Pig to Tar and Olive Oil. E. Desbaillet, Arch. internat. de méd. expér. **3**:315, 1927.

The intrapleural injection of tar and olive oil, or the emulsion of tar in olive oil, reveals tissue forming potentialities of the visceral pleura as follows: 1. The pleural epithelium hypertrophies, sometimes acquiring a brushlike effect. This absorbs the olive oil and phagocytizes the foreign particles of tar. 2. The connective tissue layer proliferates and forms an embryonal, rather verrucous or villous connective tissue often forming fungiform masses. The new tissue formation is capable of restoring the pleural epithelium. In the presence of the foreign bodies of tar, it acquires a structure similar to paraffinomas. The subpleural pulmonary parenchyma develops a hypertrophy of the alveolar epithelium after the absorption of pure olive oil. This is followed by hyperplasia and dilatation of the tubules and alveoli and connective tissue formation. This resulting adenomatous structure is attributed to the presence of the tar. The emulsion of the tar in olive oil is broken up in the pleura. The tar is engulfed by the proliferation of connective tissue and by the phagocytic action of the hypertrophied epithelium of the pleura and alveoli, and in part by the large mononuclear cells.

N. Enzer.

Digestive Leukocytosis. André Plichet, Sang **1**:134, 1927.

Plichet's report is a résumé on the subject of the work of European investigators and also the result of his rather scattered clinical observations. It

is apparently established beyond question that a digestive leukocytosis exists. It remains to elucidate its relationship to the quality of the food ingested and also its mechanism.

Plichet affirms that the digestive leukocytosis is in direct connection with the quality and quantity of the gastric juice and, therefore, with the kind of food ingested; meat causes the highest leukocytosis, next follows milk, butter and finally sugar. The leukocytosis concerns mainly the polymorphonuclear leukocytes. The variations in the number of the white cells are apparently caused by any substance which changes the blood pressure. It is possible that the vegetative system plays a rôle in the changes in the number of cells. The article is accompanied by an exhaustive bibliography.

B. M. Fried.

The Origin of Blood Platelets and the Theory of Wright. A. Perroncito, Sang. **1**:297, 1927.

Perroncito considers that Wright's theory tracing the origin of the blood platelets to megakaryocytes is proved neither from anatomic nor from embryologic or experimental points of view and that it should not be taken into consideration even as a hypothesis. He, himself, does not advance any theory or even a suggestion as to the possible genesis of this blood element.

B. M. Fried.

Primary Cancer of Lung. G. Casolo, Osp. maggiore **15**:261, 1927.

In 2,658 necropsies at Padua there were 200 carcinomas, and of these only two were primary in the lungs. In 11,968 necropsies in Milan there were 15 cases of primary pulmonary carcinoma.

Pringle's Disease. A Clinical and Histologic Contribution to Our Knowledge of the Polymorphism of the So-Called Symmetrical Multiple Sebaceous Adenomas of the Face. L. Pais, Tumori **13**:273, 1927.

Pais reports the case of a woman, aged 32, with deficient mental development and epileptiform convulsions. She had multiple symmetrical lesions on her face which, on microscopic examination, presented the picture of nevi rather than that of adenoma of the sebaceous glands. On account of the multiplicity of the histologic observations in similar cases, the author prefers the name of Pringle's disease to the various descriptive terms which have been used in the literature. The condition is evidently due to some form of embryonic maldevelopment and, as Vogt has pointed out, is almost regularly associated with tuberous sclerosis of the brain. Judging from the clinical symptoms, this cerebral lesion was also present in Pais' case.

W. Ophüls.

Strumametastasen im Auge. R. Cords and W. Eigel, Arch. f. Ophth. **118**:478, 1927.

The case is offered as the first to be reported of an adenoma of the thyroid metastasizing to the eye. A woman, aged 34, had had an enlarged thyroid gland for the last four years, and a tumor over the right brow since two years ago. The tumor of the neck was removed and diagnosed pathologically as colloid goiter. Following this, metastases appeared in the bones, and in both eyes. Autopsy also showed nodules to be present in the muscles, lungs, kidneys, suprarenals and liver. All the metastatic nodules showed a glandular structure, with small regular follicles containing colloid. A good histologic description is given of the metastatic growths in the eyes.

Benjamin Rones.

The Pathologic Anatomy of Status Dysraphicus. F. W. Brewer, Deutsche Ztschr. f. Nervenh. **99**:104, 1927.

In three of eight bodies with definite funnel-shaped breasts there was a marked gliosis of the cervical cord in the anterior half of the posterior com-

missure, in one case with cavity formation. In another case a hydromyelia was present, in two others only an increase in central gliosis, and in two cases no abnormality was noted. ["Dysraphie" used by Henneberg und Koch (Monatschr. f. Neurol. u. Psych., 1923, vol. 54) for interruption in the closure of the primary neural tube. Syringomyelia is a product of a "dysraphie."]

ROY GRINKER.

RECKLINGHAUSEN'S DISEASE WITH A PARTIAL INTRAMEDULLARY LOCALIZATION. K. WALTHARD, Deutsche Ztschr. f. Nervenh. **99**:124, 1927.

In a case with multiple peripheral nerve and root neurinomas, an extramedullary neurinoma was found and also an intramedullary one at the fifth to the seventh cervical segments.

ROY GRINKER.

THE INCREASING NUMBER OF DEATHS FROM THROMBOSIS AND EMBOLISM OF THE LUNGS. T. FAHR, Klin. Wchnschr. **6**:2179, 1927.

According to results presented the number of cases of thrombosis and embolism of the lung increased 100 per cent during the last two years. The most probable cause is the increased use of intravenous medication. The author adds that he does not consider the intravenous medication alone the only causal factor in thrombosis, but that it is rather the provoking agent added to conditions already favoring this disorder.

R. BRENNWASSER.

THE ORIGIN AND DISAPPEARANCE OF AMYLOID IN MAN. H. WALDENSTROM, Klin. Wchnschr. **6**:2235, 1927.

The clinical diagnosis of amyloidosis is made with certainty only by puncture and a microscopic examination of the tissues removed. By repeated punctures the development, the diminution and the complete disappearance of the amyloid have been followed. A liver extensively infiltrated with amyloid may become entirely free. Waldenstrom has treated three patients so diseased.

E. F. HIRSCH.

EDEMA OF THE LUNGS AFTER REMOVAL OF TRACHEAL STENOSIS. R. NISSEN, München. med. Wchnschr. **74**:1362, 1927.

Chronic dyspnea due to partial obstruction of the trachea was suddenly relieved by surgical procedure and acute edema of the lungs resulted in four instances. The massive serona transudation into the lungs was caused by the rapid unburdening of the pulmonary circulation.

J. D. WILLEMS.

THE QUESTION OF THE GRANULOCYTES. W. GERLACH, München. med. Wchnschr. **74**:1452, 1927.

This is a critical discussion of the question of the origin of the granulated leukocytes in inflammatory reactions. It is maintained that the polymorphonuclear, granulated, oxydose-positive leukocytes found in the exudate of inflammatory processes originate in the blood and the bone marrow, and leave the vessels at the site of the reaction.

J. D. WILLEMS.

FAMILIAL OCCURRENCE OF HIRSCHSPRUNG'S DISEASE. R. BUTTERSACK, München. med. Wchnschr. **74**:1626, 1927.

One of four children of the same parents and three of eleven grandchildren had Hirschsprung's disease.

BIRTH CRISES IN THE BLOOD OF NEW-BORN CHILDREN. W. BÜNGELER and P. SCHWARTZ, München. med. Wchnschr. **74**:1822, 1927.

At birth the reticulo-endothelial system of both premature and full-term children stores iron pigment. This conservation reaches its maximum two months later, and diminishes gradually. The extent of iron storage is dependent on the blood destruction at birth. This mechanism effects the late results of birth trauma hemorrhages. Blood taken from the cord at the time of birth has in a number of children, the same morphologic composition as that of the adult. The composition of the blood of those children who have changes during the first day of birth and of those born with such changes, becomes normal within three or four days. This indicates that the physiologic composition of the blood of the new-born corresponds to the normal of the adult. Changes in composition of the new-born blood are deviations from the normal and are not physiologic. There seems to be a direct relation between the duration and difficulty of birth and the degree of blood changes of the new-born. In the same way the severity of birth trauma parallels the degree of changes in the blood. The changes in the composition of the blood appear during or immediately after birth, like crises. These variations of the red and white blood cells are individually complex, and are therefore designated as birth crises in the blood of the new-born. They correspond to those crisis-like changes of the blood that appear with the resorption of extravasated or parenterally introduced blood or protein in animal experiments, and in similar condition in man. Because of this similarity, the authors conclude that the birth crises in the blood of the new-born are caused by the resorption of blood and protein. These blood and protein substances result from birth trauma. The appearance of the blood crises is dependent on the maturity of the child; in fact, are more frequent and more marked in the premature, which corresponds to the more frequent and severer lesions in this group due to trauma at birth.

AUTHORS' SUMMARY.

ANGIOMA, LIPOMA AND OSTEOMA OF THE VERTEBRAE. K. MAKRYCOSTAS, Virchows Arch. f. path. Anat. **265**:259, 1927.

Vertebral hemangioma is supposed to be a rare condition. The author claims that he could find only ten recorded cases in the literature. The reported examples have usually made themselves evident by compression of the spinal cord. That vertebral hemangiomas not associated with symptoms are not rare is apparent from the material studied by the author in the institute of Erdheim, who has been devoting especial attention to complete examination of the vertebral column. Forty-one hemangiomas were detected in twelve persons. The lesions were small, were situated in the bodies of the vertebrae, were not encapsulated and were partly thrombosed and organized. They may cause compression of the cord by distending the vertebral body or rendering it porotic or by association with an extradural hemangioma. Six small central lipomas of the vertebral body were found in four cases, three of the latter having also hemangiomas. In four cases there were six osteomas. The latter were small, measuring only 5 mm. in diameter, and were composed of dense eburnated bone. The lesions noted occurred chiefly in older persons and were more frequent in females.

O. T. SCHULTZ.

CONGENITAL ATRESIA OF INTESTINE. ALFRED TOBECK, Virchows Arch. f. path. Anat. **265**:330, 1927.

Tobeck makes two cases of congenital atresia of the intestine the basis of a discussion of the genesis of this condition. In the first case the small intestine contained three areas of occlusion and the large intestine one; and in the second case there was a membranous occlusion at the junction of jejunum and

ileum. The author does not accept fetal enteritis or amniotic adhesions as cause for the anomaly, but considers it the result of embryonic maldevelopment within the intestinal tract itself. Atresia occurs most often at those situations in which hyperplasia of the epithelium and mesodermal abnormalities of growth arise during fetal life, as determined by Tandler, Kreuter, Forssner and others. In both of Tobeck's cases partly calcified meconium bodies were present in the intestinal lumen below the sites of occlusion. Their presence can be explained only by assuming that the anomaly arises as a stenosis which permits the passage of material until after the secretion of bile is established. Complete occlusion is then followed by deposition of calcium, the calcium being excreted by the intestinal epithelium.

O. T. SCHULTZ.

CLOACAL MALFORMATION. ALFRED TOBECK, Virchows Arch. f. path. Anat. **265**: 354, 1927.

The maldevelopment described, which occurred in a full term female child who died during delivery, consisted of a greatly distended vaginal cloaca into which the urinary bladder and rectum opened. The cloaca did not open to the exterior. The uterus was duplicated and consisted of two outpouchings at the upper pole of the cloaca. The ovaries were absent. Other anomalies noted were a biventricular trilocular heart and absence of the gallbladder. The peritoneal surface of the malformed urogenital organs was covered by a layer of fibrinous exudate. The peritonitis was a later condition than the maldevelopment and had no part in the causation of the latter. Cloacal anomalies of the type described are not the result of simple inhibition of growth and differentiation during the fetal period, but are due to a more complex combination of processes consisting of mesodermal hypertrophy at the region of the anal membrane, inhibition of growth of tissues immediately above this zone and overgrowth of the higher structures.

O. T. SCHULTZ.

UNUSUAL FORMS OF VASCULAR SYPHILIS. S. S. WAIL, Virchows Arch. f. path. Anat. **265**:414, 1927.

Two unusual forms of vascular syphilis described by Wail consisted of nodular syphiltic periarteritis of the coronary vessels in a man, aged 30 years, and diffuse syphiltis arteritis of the pulmonary artery and its branches in a man, aged 25 years.

O. T. SCHULTZ.

MYOCARDITIS IN TRICHINOSIS. H. ZOLLER, Virchows Arch. f. path. Anat. **265**: 430, 1927.

In each of three patients who died of trichinosis during the fourth, fifth and eighth week of the disease, respectively, the myocardium contained multiple foci of subacute inflammatory reaction, in which eosinophils were present. The parasite could not be seen in any of the lesions. A similar reaction was produced experimentally in guinea-pigs, and here also the parasite could not be detected. Wail does not share Wehrmann's belief that the myocarditis of trichinosis is toxic in origin, but believes it to be the result of an actual invasion of the myocardium by parasites in heavy infestations, the young trichinellae disappearing early from the lesions.

O. T. SCHULTZ.

VILLOUS ENDOCARDITIS. H. KRISCHNER, Virchows Arch. f. path. Anat. **265**:444, 1927.

The slender fibrous villi, which are sometimes seen on the surface of the valves of the heart and which were first described by Lambl in 1856, are not organized thrombi, as claimed by Felsenreich and Wiesner. Occurring on valves which have been previously inflamed, they arise as the result of a

degenerative process in the collagenous tissue leading to rupture of elastic fibrils. The latter, with the surrounding degenerated material, project from the free surface of the valve. An ingrowth of connective tissue occurs from the base, and the surface finally becomes covered by endothelium.

O. T. SCHULTZ.

SICKLE CELL ANEMIA. R. H. JAFFÉ, Virchows Arch. f. path. Anat. **265**:452, 1927.

Sickle cell anemia, which is unknown in Germany, is reviewed for the German reader by Jaffé of Chicago, and a histologic study is given of tissues from two fatal American cases. The disease is considered a hemolytic anemia, which has in common with familial hemolytic icterus an hereditary factor and the occurrence of anemia with jaundice. It occurs chiefly in persons with low resistance, in whom the condition may be latent, becoming active as the result of any intercurrent disease. Sickle-shaped erythrocytes are absent from the blood during the latent stage, but can be made to appear in vitro. Active erythropoiesis and myelopoiesis were present in the bone marrow of the cases studied histologically. The nucleated erythrocytes within the bone marrow had the normal shape, but some of them had become deformed in the peripheral circulation. The change in the shape of the erythrocytes occurs in the organs of the reticulo-endothelial system, chiefly in the spleen. The altered red cells are phagocytized by the Kupfer cells of the liver. Calcium and iron incrustation of the trabeculae of the spleen was noted as the result of hemorrhage, and granules of iron pigment were present in the renal tubular epithelium, and in the Kupfer cells when erythrophagocytosis was not too great. Iron pigment was not seen in the liver cells, in the lymph nodes nor bone marrow.

O. T. SCHULTZ.

ORIGIN OF ERYTHROCYTES. W. KOMOCKI, Virchows Arch. f. path. Anat. **265**: 514, 1927.

In the turtle and salamander Komocki describes the new formation of erythrocytes from nuclei which have been extruded from other erythrocytes or which have lost their hemoglobin-containing cell body. Such naked nuclei undergo active division. The development of leukocytes from naked erythrocyte nuclei is also held to be possible.

O. T. SCHULTZ.

AMYLOID OF THE SEMINAL VESICLES. M. WINKELMANN, Virchows Arch. f. path. Anat. **265**:524, 1927.

Winklmann records two examples of amyloid change of the seminal vesicles, one in a man, aged 60 years, the other in a man, aged 70 years, both of whom gave serologic evidence of syphilis but were free from gumma. In the first case the vesicles were invaded by a carcinoma of the prostate, and in the second case by a round cell sarcoma of the prostate. The amyloid had been deposited between the epithelium and the submucosa, and had completely replaced both these layers in places. Amyloid deposition was limited to the seminal vesicles.

O. T. SCHULTZ.

A CONTRIBUTION TO THE PHYSIOLOGY OF DIGESTIVE LEUKOCYTOSIS. W. G. TSCHISHIKOW, Folia haemat. **34**:125, 1927.

Tschishikow studied the leukocytic count in dogs following digestion of different kinds of foods. He noticed that the number of leukocytes in this animal varied during the daytime without any relation to intake of food; the highest figures are found during the morning hours and the lowest during the evening. Broth and meat cause an increase in the leukocytic formula from 10,500 to 18,000 per cubic millimeter. This increase can be divided into two phases: one reaches its climax one hour and fifteen minutes and the other

four hours and forty minutes after feeding. The process of eating and swallowing and also gastric and intestinal secretion do not lead to an increase in the number of leukocytes. The passage of gastric juice into the intestine provokes a leukocytosis.

B. M. FRIED.

CLINICAL AND EXPERIMENTAL INVESTIGATION ON THE RESISTANCE OF LEUKOCYTES. JOSEF WEINAND, Folia haemat. **34**:244, 1927.

The resistance of leukocytes is usually decreased in human beings in toxic-infectious processes. In nephrectomized guinea-pigs with uremia, and also in experiments with benzol and phenylhydrazine poisoning the resistance of the leukocytes remained unchanged.

B. M. FRIED.

INVESTIGATION OF THE THREADS FOUND IN BLOOD. K. TAKEUCHI, Folia haemat. **34**:259, 1927.

Takeuchi investigated human and animal blood with particular attention to the presence of thready structures which at one time were considered as parasites causing pernicious anemia. With the dark-field illumination he was able to detect threads in the blood of practically every animal. He emphatically denies there being parasites which cause disease. They show increase in number in preserved blood, in vitro and under the cover glass under the influence of heat, toxins, etc. They disintegrate with facility furnishing a blood dust (hemokonia). Takeuchi believes that they originate from erythrocytes.

B. M. FRIED.

CONCERNING A PECULIAR REACTION OF VASCULAR ENDOTHELIUM ASSOCIATED WITH THROMBOSIS. FOLKE HENSCHEN, Acta med. Scandinav. **65**:539, 1927.

A peculiar proliferation of vascular endothelium is described, which may be associated with more or less extensive thrombosis, in certain capillary vessels with congestion and chronic inflammation of the surrounding tissue. The process is regarded as a new and hitherto undescribed form of productive thrombovasculitis. The endothelial cells grow as long and slender chains in the stationary or fluid blood and may dispart the blood. The imprisoned red cells may become changed into a hyaline mass with the morphologic and tinctorial appearance of fibrin. The most pronounced changes of this kind have been observed in urethral caruncles. The analogy of this process to the so-called endovasculitis verrucosa in typhoid fever, in certain colon bacillus infections, and sepsis is emphasized. Here also hyaline thrombi arise through proliferation of the intima and fibrinoid change of nucleated and red cells.

AUTHOR'S SUMMARY.

Pathologic Chemistry

CHEMICAL URINARY STUDIES ON PATIENTS WITH PULMONARY TUBERCULOSIS UNDER SANOCRYSIN TREATMENT. K. LUCILLE MCCLUSKEY and LILLIAN EICHELBERGER, Am. Rev. Tuberc. **16**:273, 1927.

The percentage of gold eliminated in the urine of four patients with pulmonary tuberculosis during treatment with sodium aurothiosulphate varied from 31.1 to 63.8, with an average of 45. There are decided differences in the elimination of gold in the urine by tuberculous patients following the first injection of sodium aurothiosulphate. The greatest daily elimination of gold generally occurred within from one to three days. Gold was found in the urine for from 100 to 130 days. Sodium aurothiosulphate appears to cause a disturbance in the water-balance of a tuberculous patient. The excretion of creatinine in the urine is low in patients critically ill with phthisis. The total acid (ammonia plus titratable acid) excreted in the urine of patients

with far advanced tuberculosis is below normal. The excretion of acid bodies, as estimated by the determination of total acidity, p_H and ammonia in the urine, is not altered by sodium aurothiosulphate. H. J. Corper.

Reducing Non-Sugars and True Sugar in Human Blood. M. Somogyi, J. Biol. Chem. **75**:33, 1927.

A method is presented for the determination of reducing nonsugars (residual reduction), and thereby, for the estimation of true sugar in blood. The amount of reducing nonsugars in human blood is found to be uniform, averaging 27 mg. per hundred cubic centimeters of blood in terms of glucose, as determined by the Shaffer-Hartmann method with the modified reagent. It is independent of the blood sugar level, and rises above the normal only in cases of high nitrogen retention. The distribution of reducing nonsugars in corpuscles and plasma is unequal; the average value for corpuscles is 47 mg. per hundred cubic centimeters, for plasma 10 mg. per hundred cubic centimeters. In human blood, the subtraction of 27 mg. per hundred cubic centimeters from the apparent sugar, as determined with the modified Shaffer-Hartmann reagent, gives the true sugar with a maximum error of ± 4 mg. per hundred cubic centimeters.

Author's Summary.

Changes in the Oxygen Capacity of the Blood Pigment of Rabbits Following Splenectomy. B. B. Stimson, J. Biol. Chem. **75**:95, 1927.

A nonoxygen-carrying hemoglobin appears in the blood of rabbits following splenectomy. It does not show the characteristic spectrophotometric picture of methemoglobin, and disappears from the circulation within a period of from three to six days after the operation. Arthur Locke.

On the Hydrogen Ion Determination of Normal Saliva. M. Henderson and J. A. P. Millet, J. Biol. Chem. **75**:559, 1927.

The normal p_H range of human saliva is from 6.2 to 7.6. The minimum value is manifested at the moment of arising in the morning. It then increases to a value exceeding p_H 7, occurring shortly after breakfast, quickly decreases to a value of about 6.7, slowly recovers neutrality and again becomes alkaline immediately after luncheon. [The varying composition of the saliva during this period and the possible relation of the observed variation in p_H to such a variation in composition were not studied.] Arthur Locke.

The Mineral Content of Human Skin. H. Brown, J. Biol. Chem. **75**:789, 1927.

The mineral content of the human skin changes constantly. There is a slight decrease in the silicon content and a slight increase in the calcium, magnesium and total ash contents with advancing age. Arthur Locke.

The Lipid Distribution in Normal and Abnormal Liver Tissues: I. Beef Livers. E. R. Theis, J. Biol. Chem. **76**:107, 1928.

The average lipid content of nine normal beef livers was found to be 4.6 per cent. Of this amount, 55 per cent was phospholipid, 36 per cent liquid fat and 8.26 per cent solid fat. An abnormally large liver showing distinct fatty degeneration changes contained 4 per cent total lipids of which 29.1 per cent were phospholipid, 29.1 per cent liquid fat and 40.9 per cent solid fat.

Arthur Locke.

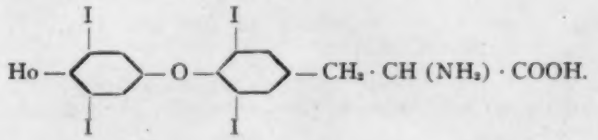
Biochemical Study of Prostato-Vesicular Secretion. Joseph F. McCarthy and others, J. Urol. **19**:43, 1928.

In normal young men the prostatovesicular secretion is high in calcium, inorganic phosphorus, hydrolyzable phosphorous and amino nitrogen. The sugar varies in amount, but in fresh semen the amount of sugar exceeds that in the blood.

Constitution and Synthesis of Thyroxine. C. R. Harington and G. Barger, Biochem. J. **21**:169, 1927. Harington, Ibid. **20**:293, 300, 1926.

Note on Physiological Test of Synthetic Thyroxine. D. M. Lyon, ibid. **21**:181, 1927.

Thyroxin is a tetraiodo derivative of the *p*-hydroxyphenyl ether of tyrosine. It is probably formed in nature by the coupling of two molecules of diodotyrosine with the loss of one side chain. The four iodine atoms may occupy the positions shown in the formula:



This compound has been synthesized by Harington and Bargen and found to be chemically identical with natural thyroxin.

The administration of synthetic thyroxin to persons suffering from myxedema results in an increase in the basal metabolic rate which is quantitatively similar to that produced by natural thyroxin.

Arthur Locke.

The Calcium-Ion Concentration During Pregnancy and Its Relation to Tetany. O. Bokelmann and A. Bock, Klin. Wchnschr. **6**:2427, 1927.

Variations in the blood calcium during pregnancy does not have any relation to tetany. The calcium supplied to the fetus is not simply by diffusion, but also by active absorption. The increased content of calcium in the blood of the mother favors the deposition of calcium in the placenta.

Authors' Summary.

CO_2 Content of the Spinal Fluid with Circulatory Disturbances. A. Schürmeyer and H. Schwarz, Klin. Wchnschr. **6**:2470, 1927.

In many patients with circulatory disturbances, just as with acidosis, there is a diminution of the carbonate of the spinal fluid (generally about the same as the blood carbonate).

E. F. Hirsch.

Microbiology and Parasitology

Brucella Bacteremia in Endocarditis. R. W. Scott and O. Saphir, Am. J. M. Sc. **175**:66, 1928.

Brucella abortus was found in the blood of a patient with acute endocarditis engrafted on chronic endocarditis.

Transmission and Cultures in Sandflies of Leishmania Tropica. S. Adler and O. Theodore, Ann. Trop. Med. **21**:89, 1927.

Of twenty-eight attempts to transmit cutaneous leishmaniasis to man from artificially infected sandflies, six gave positive results. The successful experi-

ments were carried out with *Leishmania tropica,* which had developed eight days and more in *Phlebotomus papatassii.* Nine experiments with *L. tropica* which had developed from two to seven days in *P. papatassii* all gave negative results during an observation period of from five to fifteen months. The histopathology of three lesions of experimental cutaneous leishmaniasis was found to resemble that of naturally occurring oriental sores. Specific agglutinins were demonstrated in two of the experimental cases.

The sandfly, *P. papatassii* was infected by Adler and Theodore with *L. tropica, L. braziliensis* and two strains of *L. infantum* by feeding on emulsions of parasites through a membrane of rabbit skin. In *P. papatassii,* cultures of *L. tropica* behaved exactly as *L. tropica* ingested from an oriental sore. The pathogenicity for man of culture forms of *L. tropica* was increased by passing through a sandfly. Cultures of *L. infantum* (Paris strain) behaved similarly to *L. tropica* in *P. papatassi.* In the case of a strain of *L. braziliensis* and *L. infantum* (London strain) the infection was confined to the stomach of the sandfly. Napier's formaldehyde reaction was negative with immune serum for *L. tropica, L. braziliensis* and two strains of *L. infantum.*

Experimental Echinococcus Infection in Cat and Fox. T. Sothwell, Ann. Trop. Med. **21**:155, 1927.

The cat, the fox, pigs, rabbits, squirrels, turkeys and fowl may be possible sources of infestation with hydatid. Cats, especially, like dogs, should be kept out of abattoirs.

Weil's Disease and Yellow Fever. A. W. Sellards, Ann. Trop. Med. **21**:245, 1927.

Yellow fever and Weil's disease are examples of an acute infectious jaundice. The two diseases are fundamentally different in their etiology, in their epidemiology and in their pathology. The differential diagnosis of Weil's diseases from other types of infectious jaundice can ordinarily be accomplished easily by means of the Pfeiffer reaction with leptospira. If the serum of a patient convalescent from an acute infectious jaundice gives a positive Pfeiffer test with leptospira, using either *L. icterohaemorrhagiae* or *L. icteroides,* then yellow fever can be excluded and the diagnosis of Weil's disease is justified. The disease described in West Africa as yellow fever is identical in all known respects with yellow fever of the New World. *L. icteroides* is not the causative agent of yellow fever. Prophylactic immunization, therefore, with *L. icteroides* can give only a false sense of protection against yellow fever. Purely temporary protection may conceivably be obtained by the use of serum of patients convalescent from yellow fever. In lieu of the designation Weil's disease, the name leptospirosis or leptospiral jaundice is suggested.

Oriental Sore. D. U. Owen, Ann. Trop. Med. **21**:277, 1927.

The case described by Owen was first diagnosed as acne vulgaris. Later, however, *Leishmania tropica* was found in a sore. Five months later scrapings from sores on the face and elbow were found to contain *L. tropica* in large numbers. The face was covered with nodules, many of which were ulcerated, while others were subcutaneous. The nose, eyelids and ears were involved, one nodule being in the external auditory meatus. The neck, anteriorly and posteriorly, had not escaped. There were four nodules on the chest just below the clavicular level. The dorsal surface of both hands and some of the fingers, the forearms, anteriorly and posteriorly, and elbows were also ulcerated. Two nodules had large rupial crusts. On the forehead alone, about eighty separate nodules could be counted, and several were found on the scalp. In all there were about 250 nodules on face and forehead.

THE PASSING OF DISEASE FROM ONE GENERATION TO ANOTHER AND THE PROCESSES TENDING TO COUNTERACT IT. THEOBALD SMITH, Internat. Clin. **3**:1, 1927.

"To sum up, we have seen that while the natural defenses set up through evolutionary and selective processes are not very efficient, they undoubtedly tend to save life in its earliest stages. Our observations, furthermore, intimate that when natural processes are interfered with much may transpire in the earliest days which acts either precipitously to destroy life or else to produce open disease later on in the earliest months. To what extent the events transpiring in the early days of human life are responsible for the high mortality of the first year is a problem for human medicine to solve. Perhaps our experimental results may add some information to the mass of knowledge already brought together on this subject."

AUTHOR'S SUMMARY.

A COMPARATIVE STUDY OF SMOOTH AND ROUGH PNEUMOCOCCUS COLONIES. JOHN R. PAUL, J. Exper. Med. **46**:793, 1927.

The characteristic appearance exhibited by the surface colonies of both smooth and rough pneumococci in twenty-four and forty-eight hour cultures on rabbit blood agar have been reviewed. Emphasis has been laid on the behavior and structure of the colonies formed by rough pneumococci, their frequent similarity to the colonies formed by certain strains of *Streptococcus viridans*, and their failure to undergo rapid autolysis in the first forty-eight to ninety-six hours, a phenomenon which is highly characteristic of the smooth pneumococcus colonies. With the smooth pneumococci it has been shown that "pseudo rough" colonies may be immediately produced under certain unfavorable cultural conditions, but such changes in colony morphology as these do not indicate that complete dissociation has taken place and that the organisms may be classified as true rough pneumococci.

AUTHOR'S SUMMARY.

THE OCCURRENCE OF ROUGH PNEUMOCOCCI IN VIVO. JOHN R. PAUL, J. Exper. Med. **46**:807, 1927.

In a survey of about forty rough methemoglobin-producing colonies in sputum cultures from a series of persons suffering from respiratory infections, twelve bile-soluble strains of suspected rough pneumococci have been isolated for study. Two of the twelve strains have shown both autolysis in saline solution and serologic reactions characteristic of rough pneumococci. The observations offer evidence that rough pneumococci may occasionally occur in human sputum. Their significance as regards the epidemiology of pneumococcus infections and of host response is alluded to.

AUTHOR'S SUMMARY.

STUDIES ON THE MODE OF SPREAD OF BACILLUS ENTERITIDIS MOUSE TYPHOID INFECTION. LESLIE T. WEBSTER and IDA W. PRITCHETT, J. Exper. Med. **46**:847, 1927.

Thirteen batches of mice from nine different sources were tested for the presence of mouse typhoid bacilli. Individuals from nine of the groups were found to be infected with the *B. enteritidis* type, four with the paratyphoid B, one with both, and one with neither type. With two exceptions, smooth type colonies alone were found. These results are in conformity with similar observations as reported by others and confirm the general belief that smooth colony types of paratyphoid-enteritidis bacilli prevail throughout the various stages of rodent typhoid infection.

AUTHORS' SUMMARY.

STUDIES ON THE MODE OF SPREAD OF BACILLUS ENTERITIDIS MOUSE TYPHOID INFECTION. LESLIE T. WEBSTER and CASPAR BURN, J. Exper. Med. **46**:855, 871 and 887, 1927.

The transformation process in the mouse typhoid enteritidis group is an easily reversible one, controlled in part, at least, by three factors, any of which may conceivably operate under natural conditions: temperature, which influences the appearance of mucoid forms; fluidity of culture mediums, which tends to favor rough variants; and bacteriophage, which stimulates the appearance of both variants. Since by manipulating these factors the transformation process may be incited at will in either direction, it is probably not genetic in nature.

During early stages of multiplication, single cells from smooth-susceptible, mucoid-susceptible and rough-susceptible and variant colonies do not show any differences in morphology or growth rate. Cells from eighteen to twenty-four hour single cell cultures of these various colony types possess similar oxygen absorption and cataphoretic migratory rates. In staining property, the cells from mucoid colonies appear larger, and those from rough colonies smaller, than the typical cells from smooth-susceptible colonies. Cells from bacteriophage-resistant colonies differ from those of bacteriophage-susceptible colonies in their ability to multiply luxuriantly in the presence of bacteriophage, and in their tendency to flocculate in acid solutions at from p_H 3.8 to 4.1, as well as in their low degree of virulence. Cells from smooth bacteriophage-susceptible colonies in contact with bacteriophage under conditions where multiplication is restrained may be altered so as to resemble the cells from the bacteriophage-resistant colonies. These facts furnish evidence that bacteriophage adheres to the surface of the bacterial cell and that the various cell changes and colony alterations are of an environmental rather than genetic nature.

Single cell mouse strains of *B. enteritidis* from smooth-susceptible colonies were, under the various conditions tested, of the same high degree of virulence. Two year old cultures, strains obtained both in interepidemic and epidemic periods, and "reverted" strains from variant colonies showed the same degree of pathogenicity. Single cell strains from variant smooth, mucoid, and rough phage-resistant colonies were definitely less virulent than the usual smooth-susceptible strains. The loss of virulence in each instance resulted apparently from contact with bacteriophage which rendered the individual cells incapable of multiplication in the animal tissues. A reduction of virulence was induced experimentally when washed cultures of the highly pathogenic smooth-susceptible cells were exposed to bacteriophage and thus rendered incapable of multiplication in the inoculated animals.

AUTHORS' SUMMARY.

THE MALTASE OF THE DIPHTHERIA BACILLUS. JOHN Y. SUGG, WILLIAM L. FLEMING and JAMES M. NEILL, J. Exper. Med. **46**:909, 1927.

Diphtheria bacilli possess a heat-labile, endocellular maltase, which retains its activity in sterile solutions of the intracellular substances which are liberated by physical disintegration of the bacterial cells. The proof of the maltase activity and the detection of the hexose products constitute experimental evidence that the living diphtheria bacillus attacks maltose by way of a preliminary hydrolysis.

AUTHORS' SUMMARY.

FURTHER STUDIES CONCERNING THE FILTRABLE VIRUS PRESENT IN THE SUB-MAXILLARY GLANDS OF GUINEA-PIGS. ANN G. KUTTNER, J. Exper. Med. **46**:935, 1927.

After injection of active material the virus localizes in the sub-maxillary glands of guinea-pigs, and when an active infection is developed the guinea-pigs do not respond to inoculation of the virus into the brain.

OBSERVATIONS ON THE VACCINE VIRUS. L. W. HUNT and I. S. FALK, J. Immunol. **14**:347, 1926.

Rabbits were made immune to vaccination by injections of vaccine virus, inactivated by heat, formaldehyde, and otherwise. Rabbits were also immunized passively by injection of serum from actively immunized animals. Such animals gave "immediate reaction" to vaccine virus. The virus could not be detected in filtrates from a Berkefeld N filter or a plaster of paris filter, and it could not be made visible by treatment with various concentrations of acids, bases and salts, or by immune serum.

CORYNEBACTERIUM ULCERANS: A PATHOGENIC MICRO-ORGANISM RESEMBLING C. DIPHTHERIAE. RUTH GILBERT and F. CONSTANCE STEWART, J. Lab. & Clin. Med. **12**:756, 1927.

The micro-organisms described differ from true diphtheria bacilli in the following respects: rapid change in morphology from bacillary to coccoid forms usually in twenty-four hours; liquefaction of gelatin; nonreduction of nitrates; reaction from intracutaneous injection of micro-organisms on both nomal guinea-pigs and on those immunized with diphtheria antitoxin; formation of extensive ulcers on animals inoculated subcutaneously with a living culture, and production of a soluble toxin for which a neutralizing antitoxin was prepared. The serum of the horse thus immunized showed a definite, but limited, increase in its content of diphtheria antitoxin. Although *Corynebacterium ulcerans* differs from the true diphtheria bacillus in these respects, it is doubtless a closely related species. From the evidence of pathogenicity that the cultures manifest, it seems probable that it may be of etiologic significance in some of the inflammatory or ulcerative lesions, especially those of the nose and throat.

AUTHORS' SUMMARY.

THE BEHAVIOR OF BACTERIOPHAGE IN SUGAR MEDIA. E. WEISS, J. Lab. & Clin. Med. **12**:937, 1927.

A fermentable sugar favors bacterial growth, but not bacteriolysis. A nonfermentable sugar does not have any effect on bacterial growth or on bacteriolysis. Mediums, acidified by sugar fermentation, do not have any visible effect on large quantities of phage; they favor the development of resistant bacteria, if small quantities of phage are added, and do not destroy bacteriophage, regardless of the concentration of sugar or length of incubation. If the sugar fermentation does not affect the reaction of the medium, the bacteriophage behave the same as in sugar-free medium. Bacteriophage enter the bodies of resistant bacteria of a susceptible strain but remain there inactive, and when inside of bacterial bodies can be liberated by a forty-eight hour tryptic digestion, but do not enter the bodies of nonspecific bacteria.

S. A. LEVINSON.

A MONILIA FROM THE RESPIRATORY TRACT. F. W. SHAW, J. Lab. & Clin. Med. **12**:968, 1927.

The monilia described by the author differs from *Monilia albicans* in that it does not form a honey-comb growth on dextrose agar, does not coagulate milk, and presents a different appearance during the development of the moniliform bodies. It differs more markedly from *Monilia psilosis*, which in gelatin shows a characteristic pine tree growth with fine hairlike lateral shoots extending from the entire length of the stab. On dextrose agar, *M. psilosis* produces a rough, yellow growth in contrast to the glossy, creamy-white appearance of *Monilia richmondi*.

S. A. LEVINSON.

TETANUS FOLLOWING VACCINATION AGAINST SMALLPOX, AND ITS PREVENTION: WITH SPECIAL REFERENCE TO THE USE OF VACCINATION SHIELDS AND DRESSINGS. CHARLES ARMSTRONG, Pub. Health Rep. **42**:3061, 1927.

1. Epidemiologic evidence is presented which indicates that postvaccination tetanus, when it develops, tends to follow severe primary vaccinations performed with large insertions and dressed with some type of shield or covering strapped to the site.

2. Shields and dressings are shown markedly to predispose to the development of postvaccination tetanus in monkeys and rabbits vaccinated with virus artificially contaminated with *B. tetani*.

3. A proper vaccination is defined as one in which the insertion is not over one-eighth inch in its greatest diameter, made by some method which does not remove or destroy the epidermis. Such insertions treated openly, i. e., without the use of shields or dressings strapped to the site, have never, in so far as we are aware, been followed by postvaccination tetanus. It seems probable that the adoption of these simple procedures of technic on the part of vaccinators, coupled with a proper warning to the person who was vaccinated, or his parents or guardian, concerning the dangers of home-applied shields and dressings, would eliminate tetanus as a complication of vaccination.

PURPURA OF GONOCOCCIC ORIGIN. PAUL CHEVALLIER and JEAN BOURGEOIS, Sang **1**:333, 1927.

Chevallier and Bourgeois affirm that the cutaneous manifestations of a gonococcic septicemia have a tendency to become purpuric. The clinical picture of gonococcic purpuras is polymorphic; it may run an acute, subacute or a fulminating course. The chronic cases run with or without hemorrhages of the mucous membranes. In some cases, the purpura is secondary to an erythemia; in others, it is primarily purpuric. It is usually associated with a blenorrhagic rheumatism. In a few cases, the heart and the liver were involved. In hepatic involvement a grave gonococcic jaundice occurs. Meningitis due to the gonococcus with a positive spinal fluid was also observed. The disease may also run an apyretic course. The blood pictures as seen in dry smears is apparently not specific. Sections from a purpuric spot show intradermic hemorrhages without rupturing the vessels and without thrombosis. The germ in the cutaneous lesion is intracellular and extracellular. The blood culture on bouillon-acetic fluid furnishes a positive result as a rule. The authors go into great detail concerning the diagnostic procedures. They discuss briefly the prognosis, which in most instances is favorable, and also the treatment. They state that in the presence of a fulminating purpura a gonococcic septicemia ought to be considered. The article is provided with a number of cases from the literature. There is an abundant bibliography.

B. M. FRIED.

BRONCHOSPIROCHETOSIS IN CHICKENS. P. KRAGE and F. WEISGERBER, Centralbl. f. Bakteriol. **102**:60, 1927.

The authors review the literature concerning pulmonary spirochetosis and then report an infection in several chickens in which the causative organism was a spirochete. The pathologic picture was that of a fibrinous cellular inflammation of the mucosa of the upper respiratory passages. The spirochetes appeared to belong to the *Spirochaeta morsus-muris* group and occurred in two forms. They appear to exist saprophytically in the pharynx and become pathogenic following some local inflammation.

PAUL R. CANNON.

THE INFLUENCE OF ALKALOIDS ON BACTERIA. ARTHUR HAIM and TORRES, Centralbl. f. Bakteriol. **102**:96, 1927.

Haim finds that many of the alkaloids, such as those of quinine, morphine and atropine exert a marked effect on certain bacteria in vitro, varying from a bactericidal to an inhibiting action.

PAUL R. CANNON.

INFECTION, VACCINATION AND IMMUNITY IN SO-CALLED INTERNAL ANTHRAX. K. HRUŠKA, Centralbl. f. Bakteriol. **102**:174, 1927.

Hruška finds that the careful introduction into the stomach or rectum by use of the catheter of enormous doses of virulent anthrax bacilli is without effect so long as the mucosa is uninjured. He thinks that there is no such thing as internal anthrax and that infection from the gastro-intestinal tract only arises as the result of some trauma. In the case of guinea-pigs and rabbits, anthrax bacilli introduced per os and per rectum remain in the gastro-intestinal tract as saprophytes and do not enter the blood stream.

PAUL R. CANNON.

THE RÔLE OF INSECTS IN THE EPIDEMIOLOGY OF RELAPSING FEVER. H. P. ROSENHOLZ, Centralbl. f. Bakteriol. **102**:179, 1927.

Rosenholz reports his studies of the possible rôle of *Acanthia S. Cimex lectularius* in the transmission of relapsing fever. He finds that infection of these bugs with European and African relapsing fever persists for a long time, perhaps frequently for their entire life. The spirochetes pass through the wall of the stomach into the hemolymph where they find the most favorable conditions for existence. When these infected bugs are placed on mice, infection of the mice occurs up to sixty-two days after the infection of the insect. The author then found that injection of infected blood into the hemolymph of the insect and the withdrawal of hemolymph at intervals was an excellent method of studying the persistence of the spirochetes in the bug. He also found that the excrements of the bug did not contain spirochetes.

PAUL R. CANNON.

THE QUESTION OF STAPHYLOCOCCUS SEPSIS. D. BERCHMANN and S. G. STSCHEDROWITZKY, Centralbl. f. Bakteriol. **102**:213, 1927.

The authors report that in human cases of staphylococcus sepsis with leukopenia there is a lessened degree of phagocytosis and that the hemolytic staphylococci, when injected into mice, rabbits and guinea-pigs, gave rise to a leukopenia with lessened phagocytosis. In these cases, dilution of the serum led to an increase in phagocytosis; hence they conclude that there is present in these serums an antiopsonin which resembles the amboceptor group in its properties.

PAUL R. CANNON.

THE TISSUE REACTION EFFECT OF BACTERIA: III. THE EFFECT OF STREPTOCOCCI, ESPECIALLY THE SCARLET FEVER STREPTOCOCCI. H. DOLD, Centralbl. f. Bakteriol. **102**:417, 1927.

Dold tested 160 strains of streptococci by the method of intracutaneous injection into rabbits, previously described by him. He divides them according to their effects, into three types, viz; type I, streptococci which cause only a slight erythema with only a slight infiltration; type II, streptococci which lead to a strong infiltration with deep inflammation and necrosis, but remains localized and heals in from one to three weeks, and type III, with a rapidly developing and spreading inflammation and leading to death of the rabbit within a few days. Forty strains from cases of scarlet fever belonged to types I and II.

PAUL R. CANNON.

A BARTONELLA-LIKE INFECTION OF FIELD MICE. MARGARETE ZUELZER, Centralbl. f. Bakteriol. **102**:449, 1927.

Zuelzer reports the finding of Bartonella or Grahamella inclusions in the erythrocytes of field mice, *Arvicola arvalis*, observed by her in 1917. A photograph and a colored plate illustrate the inclusions and she describes and discusses the morphology, tinctorial properties, etc., of these bodies, together with their distribution and significance.

PAUL R. CANNON.

THE QUESTION OF BACTERIOPHAGES. ERNST FRÄNKEL and ERNST SCHULTZ, Ztschr. f. Immunitätsforsch. u. exper. Therap. **51**:382, 1927.

The authors studied seven bacteriophages obtained from various sources. They all passed through Berkefeld, Reichel and Chamberlin filters and de Haven filters, numbers 1-6. Only the electronegative adsorbents had any influence on the bacteriophage, which suggests that the lysin is an electropositive entity.

PAUL R. CANNON.

DEVELOPMENT OF THE BACTERIOPHAGE FROM KILLED BACTERIA. WALDEMAR GOHS and IRENE JACOBSOHN, Ztschr. f. Immunitätsforsch. u. exper. Therap. **53**:12, 1927.

The authors found that the bacteriophagic lysin can be formed from bacteria killed by glycerol, sodium fluoride and chloroform. Bacteria killed by heat at from 57 to 58 degrees for thirty minutes do not form lysin. They believe that the formation of lysin is not a secretory function of changed bacteria, as Bordet and Doerr have suggested, but is due to specific "lysin forming autolysis" which is weaker with killed organisms than with living.

PAUL R. CANNON.

SANOCRYSIN TREATMENT IN EXPERIMENTAL TUBERCULOSIS OF RABBITS. H. BJÖRN-HANSEN, Ztschr. f. Tuberk. **49**:27, 1927.

Repeating essentially the previously reported experiments by Madsen and Mörch, the author could not observe beneficial effect of treatment with sodium aurothiosulphate on infected rabbits.

MAX PINNER.

MY RESEARCHES IN TUBERCULOSIS DURING THE YEARS OF 1918 TO 1926. A. SATA, Ztschr. f. Tuberk. **49**:116, 1927.

Guinea-pigs were inoculated with minimal amounts of live virulent tubercle bacilli. Half of the animals developed minimal tuberculosis, which terminated their lives within from four to eight months. The rest of the animals were apparently well for a period of at least ten months. When the latter animals were killed, no tuberculous alterations were found, or only swelling of lymph glands, chronic tubercles in the spleen, slight round cell infiltrations and fibrosis in the lung. When some animals were infected with a higher dose of virulent bacilli, about one half of them showed a considerable resistance. This type of immunization is dangerous on account of the death produced by the vaccine, and not sufficiently efficient as proved by the fact that only about one half of the survivors are rendered immune.

MAX PINNER.

INTESTINAL TUBERCULOSIS AND ITS RELATION TO THE COURSE OF PULMONARY TUBERCULOSIS. H. GLATZ, Ztschr. f. Tuberk. **49**:241, 1927.

In studies on about fifty cases of intestinal tuberculosis, the author came to the conclusion that four different types can be differentiated histologically. 1. There are more or less circular ulcers with gray nodules in the base and on the serosal surface. Microscopically one finds here typical epithelioid and giant cell tubercles in the lymphatic tissue. Destruction is slow, an uncharacteristic granulation tissue is formed, scar formation and tendency to healing is frequent. 2. There are less dense tubercles with edema; giant cells are rare. There is little tendency to healing, and whenever it occurs, it is incomplete. Besides lymphoid and plasma cells, leukocytes are found and cells of the same appearance as the large exudate cells in tuberculous pneumonia. 3. The individual ulcers are small, frequently confluent. The margins are undermined. Giant cells and epithelioid cells are absent; leukocytes predominate in the center and the exudative factor is predominant in the peripheral zones. There is no tendency to healing. 4. Nodular formations are absent. The ulcers represent

a diffuse caseation of the tissue, which frequently penetrates the entire thickness of the wall. The mesenterial lymph glands are frequently caseated. It is shown by these observations that intestinal tuberculosis, the same as pulmonary tuberculosis, may present every phase from the purely productive to the purely exudative and the primarily caseating type of lesion. The pulmonary lesions in these cases are generally of the same anatomic type as those found in the intestines.

MAX PINNER.

Immunology

ON ANTIGENS: ANTIGENIC PROPERTIES OF GLUE, WHEAT AND HOUSE DUST. S. G. RAMSDELL and M. WALZER, J. Immunol. **14**:207, 1927.

Le Page's glue, which is a potent atopen in human hypersensitiveness, is a poor antigen in the guinea-pig and the rabbit. Anaphylactic sensitivity in guinea-pigs injected with this substance could not be demonstrated by the intravenous method of testing; and usually only weak, submaximal contractions were obtained in the uteri by the Dale method of testing. Glue resembles the pollen type of antigen more than the egg white in the nature of the uterine contraction elicited, its slow reaction time, and in its ability to induce repeated contractions of the uterus with the same stimulating dose.

AUTHORS' SUMMARY.

INVESTIGATION OF THE CATAPHORESIS OF TOXIN AND ANTITOXIN IN THE "FIELD AND TEAGUE" AND IN OTHER APPARATUS. M. E. MAVER and I. S. FALK, J. Immunol. **14**:219, 1927.

Maver and Falk have repeated the experiments of Field and Teague, using their apparatus. Both toxin and antitoxin migrate to the cathode. Numerous natural and purified proteins were also found in the cathode agar arc when electrolyzed in solution alkaline to their iso-electric points. The authors conclude from their experimental evidence that misinterpretation of the results obtained with their apparatus led Field and Teague to conclude that toxin and antitoxin are electropositive colloids. The results of an investigation of their apparatus support the explanation that the toxin and antitoxin do not migrate to the cathode by virtue of a positive charge which they carry, but that they are swept to the cathode by the endosmotic streaming of the water. When a U-shaped cataphoresis apparatus was used, the antitoxin migrated to the anode in solutions of p_H 12.5, 9, 8.2 and 6, and to the cathode in solutions of p_H 4.6 and 3.8. Antitoxin may therefore be considered an amphoteric colloid. The toxin migrated to the anode in solutions having a p_H 9.2, 8.2 and 6.6. But the toxin was more sensitive to acidification, and the potent toxin did not migrate to the cathode or anode at a p_H of 4.9 or 4.2.

S. A. LEVINSON.

A STUDY OF DIPHTHERIA ANTITOXIC SERUM OF EXCEPTIONALLY HIGH POTENCY WITH A COMPARATIVE ANALYSIS OF ITS VARIOUS CONSTITUENTS. M. B. KIRKBRIDE and P. P. MURDICK, J. Immunol. **14**:235, 1927.

Diphtheria antitoxic serums of exceptionally high potency, namely, 2,050 units per cubic centimeter, and of low potency, 230 and 290 units, and normal horse serum were analyzed to determine quantitatively their inorganic and organic constituents. The comparative analysis of the inorganic constituents yielded fairly constant amounts with only slight individual variations, excepting possibly in the content of calcium and of sulphur. A high calcium content was found in the more potent serum. In a second series of comparative analyses of six different serums, the results did not indicate a definite relationship although a later bleeding from the horse giving the highest titered serum, taken after the potency had decreased 750 units per cubic centimeter, showed a lower content of both calcium and sulphate than was previously obtained. Compara-

tive analysis of the protein fractions showed a marked increase in the amount of pseudoglobulin in the antitoxic serums over that in the normal serum. This increase was especially noticeable in the serum of exceptionally high titer. The increase in pseudoglobulin was not accompanied by a decrease in albumin, but was entirely accounted for by the larger amount of total protein present. No significant changes in the euglobulin content were observed. The fats were present in fairly constant amounts both in the whole serum and in the globulin fraction.

AUTHORS' SUMMARY.

THE RAPID PRODUCTION OF IMMUNITY TO RICIN. M. L. ISAACS and A. H. GRANT, J. Immunol. **14**:243, 1927.

Guinea-pigs receiving a fatal intraperitoneal injection of ricin may be saved if, at the same time, they receive one to three subcutaneous injections of a weaker solution of ricin. The animals which survive develop ulcers at one or more of the sites of subcutaneous inoculation. These ulcers appear at the end of from four to six days and disappear within another seven.

AUTHORS' SUMMARY.

TRANSMISSION OF PROTEIN HYPERSENSITIVENESS FROM MOTHER TO OFFSPRING. BRET RATNER, HOLMES C. JACKSON and HELEN LEE GRUEHL, J. Immunol. **14**:249, 267, 275, 291 and 303, 1927.

Critic of Placental Permeability.—The passage of heterologous substances through the placenta is a physiologic, and not a pathologic, function. The placenta is permeable to antitoxins, precipitins, bacteriolysins, heterologous proteins, protein sensitizing antibodies, etc., in man, guinea-pigs and rabbits, but not in cows, goats and sheep. Explanation of this difference of permeability is based on histologic differences of placentas in various species: in man and rodentia a single cell membrane separates the maternal and fetal circulations, while in ruminants, three cell layers separate the two circulations.

The Rôle of Colostrum.—Work on the transmission of protein hypersensitivity by the colostrum was not found in the literature. Colostrum is an essential medium for the transmission of immunity from a mother to the new-born in ruminants (goats and cattle), but in rodentia (guinea-pigs and rabbits) and in the human species, the colostrum plays a negligible rôle in this transmission.

The Rôle of Milk.—Evidence was not found of a transmission of sensitizing proteins from the milk of nursing guinea-pigs to the suckling offspring. The literature also discloses a negligible rôle for the milk in the transfer of antibodies to the suckling, except in mice and ruminants.

Passive Sensitization in Utero.—Passive hypersensitiveness to horse serum, acquired in utero by the offspring of sensitized guinea-pigs, occurred with a high degree of regularity. This passive state is due to the transference of hypersensitiveness from the mother through the placenta, and is not hereditary. This hypersensitivity is transmitted to successive litters presumably throughout the period of fecundity of the guinea-pig, and persists for about two and a half months definitely, and occasionally for four months to a moderate degree.

Active Sensitization in Utero.—Definite active sensitization of new-born guinea-pigs can result from the passage of antigen from the mother to the fetus in utero. The close correspondence of the mother-fetus relationship in guinea-pigs with that in the human being therefore allows the hypothesis that infants manifestly allergic to the first contact with a foreign protein have been sensitized in the uterus by the placental passage of antigen from the mother's circulation.

AUTHORS' SUMMARY.

EFFECT OF PNEUMOCOCCUS CULTURE BROTH ON THE PHAGOCYTIC ACTION OF ANTI-PNEUMOCOCCUS SERUM. A. B. WADSWORTH and G. M. SICKLES, J. Immunol. **14**:321 and 328, 1927.

Immune serum on incubation with the culture broth of virulent pneumococci loses its power to promote phagocytosis of such pneumococci. This action is in some degree type specific. At the same time the immune serum lost its precipitative power.

EFFECT OF DEHEPATIZATION ON ERYTHROCYTE ANAPHYLAXIS IN DOGS. T. H. BOONE and E. M. CHASE, J. Immunol. **14**:337, 1927.

There is a primary extrahepatic factor that accounts for the immediate fall of arterial pressure in canine anaphylaxis to horse corpuscles.

EFFECT OF HISTAMINE ON THE PARENTERAL DENATURIZATION OF FOREIGN PROTEIN. W. H. MANWARING, D. H. MARINO and T. H. BOONE, J. Immunol. **14**:341, 1927.

Intravenously histamine delays the parenteral denaturization of foreign proteins, and this action cannot be regarded as inconsistent with the rôle of enzymes in the detoxication of foreign protein.

SKIN REACTIONS IN THE NORMAL AND HYPERSENSITIVE GUINEA-PIG. R. W. LAMSON and MAXY ALICE POPE, J. Immunol. **14**:365, 1927.

The responses to intracutaneous injections differ so greatly in the guinea-pig from those in man that they are not interpretable on the same basis.

THE BOVINE TUBERCLE BACILLUS IN IMMUNIZATION. S. L. CUMMINGS, Tubercle **8**:459, 1927.

In questions of immunity, stress should be laid on the differences between "mammalian" and "other" tubercle bacilli rather than between "human" and "bovine" types. It is unscientific and misleading to speak of "antagonism" between human and bovine infections. There is some justification for speaking of an "antagonism" between previous infection, and subsequent reinfection with mammalian tubercle bacilli, whether human or bovine. While it is true that previous infection raises the resistance against subsequent reinfection, the "immunity" so produced is merely relative, never absolute, and is often manifest only in a more favorable or more chronic type of disease. At the same time it appears certain that this relative immunity is of profound importance as a factor in the fall in the tuberculosis death rate and in the amelioration of the clinical type seen in recent years. The suggestion sometimes made that the drinking of unknown quantities of bovine bacilli in infected cows' milk is to be advocated as an aid toward stamping out human tuberculosis is dangerous and unscientific.

H. J. CORPER.

CUTANEOUS PASSIVE ANAPHYLAXIS IN HUMAN BEINGS. PASTEUR VALLERY-RADOT and PAUL GIROUD, Ann. de méd. **22**:260, 1927.

The phenomenon of passive anaphylaxis can be easily induced in animals. From a few reports in the literature it appears that analogous to the experimental animal, human beings are also liable to be sensitized passively. The authors conducted experiments on thirty-eight persons passively sensitized to the pollen of hay-fever. They obtained thirty-six positive intradermal tests and two negative. From the point of view, the results indicate that the cells of the derm are impregnated with a specific antibody which is present in the serum of sensitized persons. The "conflict" between the antigen and the antibody is thus fixed on the dermal cells and it manifests itself in the cutaneous reaction.

B. M. FRIED.

BIOLOGIC METHODS FOR THE DIAGNOSIS OF THE HYDATID CYST. E. BURNET, L. CAILLON and G. BRUN, Arch. de l'Inst. Pasteur de Tunis **16**:291, 1927.

The authors report diagnostic results secured by studies of eosinophilia, by the precipitin reaction, by the intradermal reaction, and by complement-fixation methods. The frequent presence of helminthiasis in locales where the echinococcus exists makes the eosinophil examination of doubtful value; the precipitin reaction appears indifferent; the intradermal reaction is neither constant nor specific; the complement-fixation reaction when properly standardized seems the most reliable method.

M. S. MARSHALL.

OBSERVATIONS AND RESEARCH ON THE HEMAGGLUTININS OF MOTHER AND FETUS. M. PROSPERO and G. MORRA, Arch. per Sc. méd. **49**:714, 1927.

The blood group of the child is completely fixed and manifest at birth. Fetal iso-agglutinin is not derived from the mother, but develops in the fetus during intra-uterine life and is generally of low concentration at birth. Isolysin is weak and its demonstration difficult. The permeability of the placenta does not affect the blood grouping. No difference of weight was found for children born of mothers belonging to a different group from that of the child.

AUTHORS' SUMMARY.

NEW TYPHOID VACCINE. N. BRUNI, Igiene Moderna **20**:261, 1927.

The Italian army has adopted a typhoid lipovaccine. The excipient is a vegetable oil. The change has done away with abscesses and other complications observed after the use of the old petrolatum vaccine. Only slight reactions occurred in about 30,000 soldiers vaccinated. In 100 of the group, the size of the spleen was determined after vaccination; in about half a moderate swelling was detected. Most of those vaccinated develop agglutinins of a rather high titer (1:320) after eight days. These agglutinins usually disappear in about two months. The agglutinin titer is lowest for paratyphoid A. In some persons the complement-fixation test becomes positive. In rabbits blood serum neither agglutinates nor deviates the complement after one injection of vaccine. In persons with abscesses or negative agglutination after injection, revaccination should be tried.

BLOOD TYPES AND PREDISPOSITION TO DISEASE. L. HERMANNS and J. KRONBERG, München. med. Wchnschr. **74**:967, 1927.

Four hundred and two patients are tabulated as to blood types and carcinoma and diseases of the nerves, the stomach and the internal secretory glands. The conclusion is that there is no relation between disease and blood type.

J. D. WILLEMS.

THE ACTION OF LIGHT ON COBRA VENOM. H. MUCH, PEEMÖLLER and HAIM, München. med. Wchnschr. **74**:1365, 1927.

Cobra venom in a 1:5,000 dilution lakes human erythrocytes in two hours. After exposure to mercury quartz light it will not destroy them in a 1:2,000 dilution in twenty hours. No conclusions are drawn. Additional studies concerning the absorption spectrum of the venom before and after exposure to the light, and regarding the action of cholesterin and lecithin on the poison are under way.

J. D. WILLEMS.

THE DIAGNOSIS OF RABIES BY THE PRECIPITATION REACTION. PIUS LÄSSER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **53**:1, 1927.

Lässer attempted to secure a precipitation reaction between serum from rabbits injected with various rabies viruses tested against rabies brain emulsions

as well as normal brains and brains from animals infected with encephalitis and herpes viruses. However, he found no specificity, there being precipitation with various neurotropic viruses besides rabies virus and even at times with normal brain emulsions.

PAUL R. CANNON.

THE VALUATION OF THE ANTIGENIC PROPERTIES OF THE DERIVATIVES OF DIPHTHERIA TOXIN BY MEANS OF THE RING PRECIPITATION METHOD. E. HOEN, L. TSCHERTKOW and W. ZIPP, Ztschr. f. Immunitätsforsch. u. exper. Therap. **53**:20, 1927.

The authors describe experiments as to the antigenic nature and properties of diphtheria toxin and anatoxin as influenced by heat and H-ion concentration. They find, in the case of diphtheria toxin, that heating leads to a proportionate loss of both antigenic and precipitating properties, whereas the antigenic properties of anatoxin are not so seriously impaired by heating until a temperature of from 60 to 65 degrees is reached. A p_H of from 8.4 to 6 does not influence the precipitation reactions of diphtheria toxin by the ring method. The authors feel that their method is superior to Ramon's flocculation method.

PAUL R. CANNON.

THE LATENT PERIOD IN PASSIVE ANAPHYLAXIS WITH IMMUNE SERUM OF THE SAME SPECIES. E. FRIEDBERGER and S. SEIDENBERG, Ztschr. f. Immunitätsforsch. u. exper. Therap. **53**:39, 1927.

The authors succeeded, by repeated intensive parenteral injection in guinea-pigs of foreign species protein followed by injection of their serum into previously sensitized guinea-pigs, in getting passive anaphylaxis without an incubation period.

PAUL R. CANNON.

THE SIGNIFICANCE OF LIPOIDS IN BIOLOGY AND IMMUNITY. LAJOS SURÁNYI, Ztschr. f. Immunitätsforsch. u. exper. Therap. **53**:74, 1927.

This paper is largely a discussion of the chemistry of cholesterol with its possible rôles in the animal body in health and disease. Some experiments also indicated that cholesterin and lecithin, when fed to rabbits, lead to a lymphocytosis and a neutrophilia, respectively. Immunization of a cholesterin-fed rabbit gave a better response than with a lecithin-fed one, the latter being poorer in antibody content than a normal rabbit not fed lipoids of any kind. Cholesterin also appeared to aid in preventing anaphylactic shock in guinea-pigs. Cholesterin feeding led to a decrease in complement. Narcosis led to a similar result. A pronounced atheromatosis was produced in a rabbit by feeding cholesterin for three months.

PAUL R. CANNON.

PRECIPITIN CURVES FOLLOWING INJECTIONS OF VARIOUS ANTIGENS. I. ASAI, Acta Dermat. **10**:419, 1927.

White of egg, human and other serums give different precipitin curves.

SKIN TRANSPLANTS IN RELATION TO BLOOD GROUPS. K. MATSUDA, Arch. f. Jap. Chir. **4**:1, 1927.

The best results in skin transplantation were obtained with autotransplants and homotransplants, provided the donor and the recipient belonged to the blood group.

Tumors

MALIGNANT TUMORS OF THE TESTICLE. J. H. MORRIS, Arch. Surg. **15**:530, 1927.

A young man died of visceral metastases of an embryonal carcinoma of the testis. One of the metastases was characterized by cells of the seminomatous type. Morris reports this case as one which supports the theory of the

teratomatous origin of tumors of the testicle, showing that they may develop metastases characteristic of "Chevassu's" tumor or seminome. N. ENZER.

SUBUNGUAL MELANOMA. HUTCHINSON'S MELANOTIC WHITLOW. N. A. WOMACK, Arch. Surg. **15**:667, 1927.

The three cases described bring the total number of these tumors to twenty-four. All three presented darkly discolored ulceration of the nail-bed. Metastasis to the regional nodes may occur. The tumor has little stroma and is made up chiefly of spindle cells with occasional larger polygonal ones. The pigment is both extracellular and intracellular. Bloch thinks the tumors are of an epithelial origin.

N. ENZER.

THE INHERITANCE OF SUSCEPTIBILITY TO TAR-INDUCED TUMORS IN THE LUNGS OF MICE. CLARA J. LYNCH, J. Exper. Med. **46**:917, 1927.

The conception that susceptibility to pulmonary tumors is hereditary seems to be upheld by the fact that the two strains of mice described differ conspicuously in respect to the rates of spontaneous tumors under ordinary laboratory conditions; the strains differ also under experimental conditions, as described in this report; and when crossed, the offspring by suitable back-crosses, will again show significant differences.

AUTHORS' SUMMARY.

A HISTOLOGIC STUDY OF A FEMORAL METASTASIS FROM A MYOSARCOMA OF THE UTERUS. G. GRYNFELTT, Bull. de l'Assoc. franç. p. l'étude du cancer **16**:447, 1927.

Older writers believed that the malignant transformation of myoma was in reality the result of an invasion of the benign muscle tumor by a sarcoma originating from connective tissue. In the case reported by Grynfelt, a metastasis from a myosarcoma was found within the femur. This, according to Grynfelt, represents a striking demonstration of the transformation of the muscle itself into a sarcoma. The authors give in detail the histology of the tumor.

B. M. FRIED.

A VOLUMINOUS SACROCOCCYGEAL CHONDROMA. REYNES, H., and ROUSLACROIX, Bull. de l'Assoc. franç. p. l'étude du cancer **16**:434, 1927.

The author gives a detailed report of an enormous chondroma, measuring 59 cm. in diameter, occurring in a man, aged 68.

B. M. FRIED.

A CASE OF A PRIMARY TUMOR OF THE LYMPH GLANDS OF RETICULO-ENDOTHELIAL ORIGIN. G. PUJOT, Bull. de l'Assoc. franç. p. l'étude du cancer **16**:627, 1927.

Pujot reports a case in which a cervical tumor accompanied by swelling of numerous lymph glands occurred in a baby, aged 13 months, which on histologic examination was found to be composed of "reticular and endothelial" cells. The large tumor itself was nothing other than a cervical lymph node in which the new growth was confined to the element of the reticulum. The author calls attention to the fact that in rare instances the proliferation of lymph nodes may be due not to lymphoid elements, as is usually the case, but to the reticulo-endothelial elements of these structures. Such cases ought to be designated, then, not lymphadenitis but reticulo-endotheliose (the "ose" indicates the multiplicity of foci of proliferation).

The detailed histology of the case is followed by a comprehensive discussion.

B. M. FRIED.

INCLUSION BODIES IN A CASE OF DOG SARCOMA. FRANCESCO SANFELICE, Centralbl. f. Bakteriol. **103**:415, 1927.

Sanfelice describes nuclear inclusion bodies which he found in tumors of dogs diagnosed as round cell sarcoma. Two plates illustrate the observations. He compares these with similar ones found in other disease conditions, such as certain tumors in amphibia, in the Bornasch disease of horses and in rabies, chickenpox, etc., and suggests that the observations in sarcoma in dogs point to the possibility of a filtrable virus.

PAUL R. CANNON.

INFECTION, PARASITISM AND TUMOR FORMATION. PATHOLOGIC PART. MAX BORST, Verhandl. d. deutsch. path. Gesellsch. **22**:6, 1927.

Regarding blastomas as manifestations of autonomous cellular growth and considering that normal growth is not of parasitic origin, Borst believes that the theory of the parasitic origin of tumors is difficult to understand. The existence of transitions from normal to all types of pathologic growth makes it probable, moreover, that all disturbances of growth result from a disturbance of factors controlling the normal growth. Even the destructive growth of the malignant blastomas has its physiologic pattern in the invasion of the decidua by the chorio-epithelial cells. A further defect of the parasitic theory is seen in its restriction to the origin of the malignant tumors, in spite of the fact that benign and malignant growth are of the same nature. The theory cannot be applied to teratoid malignant blastomas. Bacteria and parasites usually possess an affinity to special tissues, a universal virus had to possess a pan-affinity. Against the existence of multiple virus for the different types of tumors Borst cites the occurrence of carcinosarcomas, the formation of sarcomas after implantation of carcinomas and vice versa, and the observation of tumors of different structural type in the same organ. The parasitic theory cannot explain satisfactorily the great variations of the structural composition of blastomas nor the malignant degeneration of restricted groups of cells in teratomas. Micro-organisms and parasites found in tumor cells are in general without etiologic significance. The preservation of the specific function of the original tissue in the blastomas is a factor which does not corroborate the infectious theory, because infections formerly interfered with the function of the invaded tissue. The absence of any specific effect of the supposed virus on the stroma of tumors represents a point against this theory. It fails also to explain the gradual development of benign regenerative, hyperplastic, inflammatory proliferations into malignant tumors, processes which can be reproduced by non-infectious agents; furthermore, the occurrence of expansive, infiltrative and destructive types of growth and of mixtures of normal tissue and blastomatous tissue of the same type in malignant tumors. The absence of bacteria and parasites in metastases of carcinomas produced by these organisms and the development of metastases from cells of the original tumor are not in favor of the parasitic theory. A specific humoral reaction as existing in other infectious diseases cannot be demonstrated. The transplantation of tumor tissue follows the rules of that of normal tissue, while the inoculation of infectious material is not bound to such an extent. Borst does not believe that the transmission of Rous' sarcoma with cellfree material is definitely proved. The occurrence of congenital tumors, especially those with atavistic features and the hereditability of certain kinds of tumors, are also factors not in favor of a specific infectious origin. The tumor disease is not contagious, and the secretion and the cellular material of tumors are not infectious. The infectious nature of endemics of tumors is unproved. Infectious granulomas are reaction products of the mesenchyme against the specific micro-organisms; infiltration and destruction of these products are secondary processes due to bacterial toxins. Tumors are primary active products of all kinds of tissue, proliferating without regard to the welfare of the host organism. Experimental investigations demonstrated the possibility of tumor production by various exogenous

means of animated and unanimated nature causing always the same gradual transformation of normal cells into tumor cells without regard to the character of the causative agent. The "irritation theory" of Virchow is still the most satisfactory one, but it has defects also. Factors representing individual, racial and organic disposition may contribute in the etiology of tumors. The long interval between local irritation and end-effect points to the existence of general disturbances. In conclusion, Borst emphasizes the point that the tumor disease is not due to a single cause but represents a complex of conditions, resulting from disturbances of cellular, organic, systemic, endogenous, local and general, and exogenous factors.

WILLIAM C. HUEPER.

INFECTION, PARASITISM AND TUMOR FORMATION. CLINICAL PART. SCHMIEDEN, Verhandl. d. deutsch. path. Gesellsch. **22**:21, 1927.

Discussing the clinical aspect of this problem, Schmieden asserts that all clinical considerations and a review of the total clinical literature on the subject do not bring one reliable proof of the infectious or contagious cause of tumor formation. The infectious theory originating mainly from and supported by clinicians has at present only a few supporters and is still loosing ground. Tumors and infectious diseases take a different course. Confusion is produced by the frequent association of tumors with inflammatory processes. Tumors do not produce a general reaction, fever, general feeling of sickness, etc., as infectious diseases do. Tumors have, instead, a characteristic stage preceding the disease and developing only eventually into a neoplasm. Blastomas do not respond to any medication of specific, nonspecific and general nature. Infectious diseases do not produce a mortality of 100 per cent as carcinomas do. In infectious diseases the number of micro-organisms increases till death results, while the micro-organisms used in the production of experimental carcinomas usually have disappeared from the tissue at the time of death. Infectious diseases have characteristic stages in their course. They show a periodicity of the single disease and an epidemic character in mass infection. They usually start multicentrically while tumors in general begin unicentrically. In infectious diseases the infecting micro-organism is foreign to the body, is not species specific, does not prefer certain ages and is the main and leading element of the disease, while in tumors the blastoma cells originate from parts of the body, are species specific and are pathologic manifestations usually of certain periods of life. Congenital tumors in children of healthy parents are not under any circumstances of infectious origin. The body does not defend itself against the tumor as it does against any other infection. An endemic occurrence of tumors is not definitely proved and may have other than infectious causes, as for instance hereditability and occupational influences. Neoplasms prefer organs with increased metabolism and with cells of high proliferative ability, which are exposed to frequent mechanical lesions with resulting regenerative processes. Nonspecific chronic irritation and regeneration is also the causative agent in the production of tumors by the many described specific cancer parasites and micro-organisms. Exogenous factors, as those resulting from cultural habits, and endogenous factors, as disturbances of the endocrine metabolism, may contribute to the cause of tumor formation. But the tumor disease is mainly a local disease. Schmieden recommends the study of the precancerous diseases as the most valuable source for information of the formal genesis of tumors.

WILLIAM C. HUEPER.

INFECTION, PARASITISM AND TUMOR FORMATION. EXPERIMENTAL PART. TEUTSCHLAENDER, Verhandl. d. deutsch. path. Gesellsch. **22**:37, 1927.

Successful experiments offer the only conclusive evidence in regard to the etiologic significance of parasites and micro-organisms for the origin of tumors. Fibiger produced carcinomas of the squamous epithelium of the stomach and

tongue of rats after feeding them with the round worm *Gongylonema neoplasticum* which invades the mucosa of the stomach. Yokogawa caused carcinoma of the esophagus of rats after feeding them with *Gongylonema orientale.* Bullock, Curtis and Rohdenburg succeeded in producing sarcomas of the interstitial tissue of the liver of rats after their infection with *Cysticercus fasciolaris.* The results of these experiments rendered absolute evidence of the etiologic relation between parasitism and true malignant tumors of the rat. But with the exception of mice no other animals responded to these infections with the production of blastomas. Tumor formation in rats or mice after infection with micro-organisms was reported by Jensen, who worked with pseudo-tubercle bacilli of cattle enteritis and Blumenthal, who used strains of *Bacillus tumefaciens* and *Bacillus pyocyaneus* usually injected with the addition of infusorial earth and lymph. Nuzum demonstrated gram-positive diplococci in carcinoma, results which could not be repeated by Kross; and Glover reported the production of carcinoma in various animals after infections with a gram-positive micrococcus which he was able to culture from carcinomas of various organs in human beings. Also these experiments could not be duplicated by some other workers using similar micro-organisms. Microscopic and clinical observations support the etiologic significance for tumor formations in animals of the following parasites: *Trichodes crassicauda, Hepaticola gastrica, Fasciola hepatica,* larvae of *Oestrides* and mites of *Cnemidocoptes;* and in men of the following: *Opisthorchis felineus, Bilharzia haematobia* and *Schistosomum japonicum.* Experiments and observations on spontaneous tumors show that in addition to chemical and physical noxious factors also various endoparasites and ectoparasites and micro-organisms of vegetal and animal nature may produce or contribute to the origin of blastomas. But the animated factors are not the real cause of tumor formation. A "specific factor" is the etiologically most important element. The supporters of the parasitic theory believe that it is a microorganism living in symbiosis with the tumor cells. Teutschlaender considers the possibility of an invisible, strictly histiotropic, filtrable aphanozoon living in symbiosis with the blastoma cells. The transmission of Rous' chicken sarcomas can be explained in three different ways: common transplantation of unusually resistant and flexible tumor cells, subcellular transplantation through bioblasts and inoculation of "malignancy ferment" present in the tumor cells. Transplantation of cells with powdered, glycerinated and filtrated tumor material is possible according to investigations of Nakahara. Similar sarcomas were produced by Landsteiner and Murphy with injected embryonic material and by Fischer with normal cells changed into malignant cells in tissue cultures. Teutschlaender believes that the supposition of a "malignancy ferment" similar in character to the lytic principle of d'Herelle and produced by the tumor cells offers the best explanation of the nature of these processes. The experiments of Carrel and Fischer are considered as proofs against the infectious nature of Rous' tumors which is supported by the experiments of Gye. A generalization of these results on other tumors is unwarranted. Teutschlaender proposes to call Rous' tumors sarcoses to differentiate them from true blastomas and simple granulomas. Parasitic tumors belong to the same group of blastomas as those caused by other exogenous chemical agents. The carcinomas are not infectious, but the precancerous diseases are infections occasionally. This indirect contagiousness may explain the endemic occurrence of tumors. The purely endogenous origin of tumors has been observed (Maud Slye, Loeb). Disposition to cancer formation may be inherited. Carcinomas are neither infectious nor contagious.

WILLIAM C. HUEPER.

REGENERATION TUMORS. B. FISCHER-WASELS, Verhandl. d. deutsch. path. Gesellsch. **22**:70, 1927.

A man, aged 28, developed, after repeated treatment with roentgen rays for chronic eczema of both hands, a myxomatous fibrosarcoma on one hand and a squamous cell carcinoma on the other one.

WILLIAM C. HUEPER.

LIPOID METABOLISM IN RABBITS WITH TAR CARCINOMA. T. SHIMODA, Acta derm. **10**:325, 1927.

The growth of tar carcinoma of the skin seems to go hand in hand with the increase of cholesterol in the blood.

Medicolegal Pathology

THE RELATIVE TOXICITY OF BENZOL AND ITS HIGHER HOMOLOGUES. JOHN J. BATCHELOR, Am. J. Hyg. **7**:276, 1927.

As methylation increases from toluene to xylol and benzine with a high flash point, a decreased toxicity for rats was noted following intraperitoneal or subcutaneous injection or inhalation. All three were much less poisonous than benzene which causes marked destruction of leukocytes and of the tissues concerned with the production of other cells of the blood. These three homologues of benzene, toluene, xylol and the benzene used (boiling point 156 C.) apparently have a stimulant action for bone marrow and tend to cause its hyperplasia. The loss of weight in rats with benzene was also found to be progressively less with the increase of methyl groups in the substances used.

Benzene also acts as an irritant to the nervous system causing convulsive twitching and profound tremor. Such symptoms follow small doses and also are observed early when doses are given large enough to cause a subsequent narcosis. The lessened volatility as methylation is increased is believed to be one of the reasons for diminution of the poisonous symptoms, since those with the lower boiling points are more rapidly absorbed. Large doses of toluene and xylol, however, act as lethal narcotics.

The outcome of the results observed is a recommendation that when these homologues can be used in industry, they should be preferred to benzene because with their higher boiling points there is much less danger. The concentration required to produce a fatal poisoning with xylol, for example, is entirely an artificial and experimental condition not likely to be met with as an accident in industry.

E. R. LE COUNT.

PULMONARY EMBOLISM COMPLICATING PREGNANCY, LABOR AND THE PUERPERIUM. E. E. BUNZEL, Am. J. Obst. & Gynec. **13**:584, 1927.

From the records of three hospitals in New York, it was found that pulmonary embolism had occurred in 32 of the 31,716 women cared for on account of pregnancy. This embolism was three times greater in operative than in normal deliveries. It occurred in 2 per cent of all those with placenta praevia, and in 1.5 per cent of those with cesarean section.

Among those who had the embolism during the early months of pregnancy, there were six in whom it followed abdominal operations for complications; four of these died. Another woman suffering from heart disease had the embolism during the fourth month of pregnancy and went safely through labor and the puerperium. A second with heart trouble died from embolism before labor began.

The remaining twenty-four were delivered during the eighth or ninth months' of pregnancy, and the embolism was postpartum. The symptoms came on immediately after delivery in six, in the first twenty-four hours in two, from the third to the ninth day in seven and after the twentieth day in two. Sixteen of the twenty-four women died, making twenty-one deaths (66 per cent); there were only two postmortem examinations.

E. R. LE COUNT.

METHYL SALICYLATE POISONING: REPORT OF A CASE. DOUGLAS P. ARNOLD and A. WILMOT JACOBSEN, Bull. Buffalo Gen. Hosp. **5**:44, 1927.

A child, aged 10 months, died sixteen and one-half hours after swallowing a certain amount of methyl salicylate. After death, examination revealed

hyperemia and small hemorrhages of the brain, hyperemia of the lungs, spleen, liver and kidneys, fatty changes in the liver, edema of the lungs, and inflammatory changes in the stomach. Salicylic acid was recovered from the bile, liver, muscle, kidney and urine. The outstanding clinical symptoms were stupor, increased reflex excitability and hyperemia with odor of acetone on the breath.

FATAL POISONING BY BORAX. J. BIRCH, Brit. M. J. **1**:177, 1928.

The case of an infant, 18 days old, who swallowed 5.6 cc. of sodium borate and boric acid (as honey and borax and glycerin of borax to prevent thrush) is reported. Death was preceded by coma. The muscles and arterial blood were pink, but otherwise there were no special gross changes in the organs.

ACUTE PHOSPHORUS POISONING. C. F. SWINTON, Brit. M. J. **1**:1080, 1927.

A woman, aged 37, swallowed a teaspoonful of phosphorus mice paste five days before she died. In the meantime jaundice gradually developed with enlargement of the liver. After death, small hemorrhages were found over the lungs, in the papillary muscles of the heart, the pericardium, the diaphram and elsewhere; the liver was large, fatty, and the abdominal organs had a strong garlic odor; the kidneys were degenerated.

SEPTIC EMBOLISM FOLLOWING URETHRAL DILATION. REYNARD, Lyon méd. **139**:478, 1927.

In one patient, an abscess near the right scapula developed four days after a second dilation of the urethra. In the second patient, an abscess formed in the right deltoid region twelve days after a third dilation. Staphylococci were found in the pus of the first abscess, and the pus of the second was not examined. In spite of the intervals of four and twelve days, the abscesses were regarded as embolic because fever and severe chills occurred in both patients. The dilation was gentle and gradual, the strictures both in the membranous portions of the urethra.

E. R. LE COUNT.

TRAUMATIC RUPTURE OF THE HEART WITHOUT HEMOPERICARDIUM. V. CESARIS DEMEL, Arch. di antrop. crim. **47**:453, 1927.

In the case described there was no hemorrhage into the pericardium because the rupture of the wall of the heart extended only to the epicardium.

THE CHANGES IN WOUNDS OF THE SKIN OF DOGS MADE BEFORE AND AFTER DEATH BY DROWNING. VILMA MARK, Arch. di antrop. crim. **47**:474, 1927.

The extent and character of the changes depend on how long before drowning the wound was made and to a large extent also on the length of time that the body remains in the water.

IDIOSYNCRASY AND ANAPHYLAXIS AS RELATED TO LABOR. GIOVANNI GIOLI, Arch. di antrop. crim. **47**:616, 1927.

Intolerance in certain persons to certain foodstuffs, drugs, general and local reagents was well known to the ancients and was explained by them, as a special constitutional diathesis, called idiosyncrasy. How true this observation was is proved by the case of bronchial asthma. Richet's discovery of anaphylaxis in 1922 is applicable to the study of certain phases of individual intolerance, taking as a type, bronchial asthma. A differentiation between anaphylaxis and idiosyncrasy is attempted in the following definition. Anaphylaxis has its origin in a protein or colloid substance. It gives rise to specific reactions and has an affinity for preformed antibodies and their specific antigens; it requires a period of incubation for the preparation of sensitiveness and displays the anergic phenomenon of Pirquet and is capable of a

passive transmissibility from supposedly sensitized to immune persons. Idiosyncrasy is defined as the property deriving its characteristics from a protein, but likewise from a crystalloid substance, without regard to antigens. It is not preceded by the period of incubation. It possesses a hereditary character suggesting functional stigmas of a nervous or dyscrasic kind. It lacks a period of anergy and a demonstrable passive transmissibility. However, Gioli admits that the differentiation is not clearcut. It is sufficient to state that certain persons present phenomena of morbid hypersensitiveness to chemical, vegetable, animal substances, and to parasites and furthermore, that there is a possibility of preparing artificial antigens and that recent researches in anaphylaxis have their origin in the study of hay-fever. This is followed by an extensive historical review of the subject. Experimental anaphylactic phenomena express themselves in mucocutaneous, respiratory, circulatory and hematologic manifestations, as well as in serologic changes, such as disappearance or rapid diminution of the complement and of precipitins. He adds a personal observation of two laborers unaccustomed to field work, of previous good health who, while handling dry hay, developed on the same date and almost the same hour, edema of the face, intense conjunctival hyperemia and coryza. In one case, a small ulceration on the mucous membrane of the right nostril was noted. In the second case, a fissure in the nasal mucosa was seen. These two cases present typical anaphylactic phenomena due to the pollen of dried hay. In the third case, erythema of the face with intense conjunctivitis and coryza developed in a tin worker while carting dried reeds. When discussing the question of liability, Gioli does not find any answer in the literature as to whether such a sickness is to be regarded as an occupational risk or whether it is to be considered as an etiologic trauma in the course of occupation. He concludes that such cases should be covered by compensation even though they are the consequence of a certain morbid intolerance.

Relation of Trauma to Neoplasm Considered from a Medicolegal Point of View. F. Ballotta, Arch. di antrop. crim. **47**:661, 1927.

The recent creation of an institute of workmen insurance in Italy brings to the fore new problems in social medicine, among them the interesting question of the relation of injury to new growth. Two cases are reported. Case 1 is that of an endocranial tumor following an injury to the head sustained in a fall. Two months after the accident the patient began to suffer from an intermittent headache which became more and more severe and was confined to the right side. Later, vomiting appeared, a sense of tingling and anesthesia of the left side of the body and disturbance of the sense of equilibrium. Later loss of weight and cachexia supervened. She was tormented by the terrific headache and implored for help. A roentgenogram did not reveal a fracture of the skull. An occipital abscess, the result of a hematoma, was suspected. Death from cachexia took place seven months after the injury. Necropsy did not show any external evidence of injury to the head or body and no evidence of a fracture. The brain revealed hydrops and dilatation of the ventricles, hyperemia and stasis of cerebral vessels and of the finer intracerebral ramifications. The entire lateral and inferior part of the right temperosphenoidal lobe in its anterior two-thirds was invaded by an ovoid tumor the size of a small orange. The tumor was adherent to the dura covering the superior margin of the petrous portion and the corresponding portion of the cerebellum. The dura showed inflammatory thickening without any evidence of calcareous degeneration. No metastases or any other lesion were found. This neoplastic growth, apparently a sarcoma, consisted of compact masses of fusiform cells with an oval nucleus.

Case 2 was that of a tumor of the knee following an injury. A semispheric tumor of fibrous consistency, the size of a hazel nut, was noted in a man, aged 44, seventy-five days after an injury to the right knee. Four and

one-half month later the knee increased in volume and the tumor became softer and fluctuated. From then on the process receded and he was able to return to work. A second injury to the same knee was sustained followed by a rapid enlargement and severe pain in the knee. Resection of the joint for a suspected malignant condition was carried out. Death resulted from pulmonary complications. Necropsy showed that death was caused by extensive metastases of the lung. The growth was sarcomatous in nature. In both cases the benefit of the doubt was given the victim and not the defendant. These two cases suggest that trauma per se can cause a neoplasm. It is probable, however, that its effect is due to stimulation of proliferation in an aberrant embryonal group lying dormant in normal tissue. It may also be a factor in creating a locus minoris resistentiae. There is no evidence on hand that it may cause a benign tumor to become malignant other than the taking on of a rapid growth. The medical expert must be careful in his attempt to establish the priority of injury to trauma. The probable causal connection requires rigorous research and critical judgment of the facts by which to be guided. The expert must resist the popular tendency to ascribe to each injury a causative significance; he must likewise reject insufficient scientific observations. Serene and objective evaluation only of all the evidence at hand is conducive to a just and impartial medicolegal opinion.

TWO CASES OF TRAUMATIC RUPTURE OF THE ALIMENTARY CANAL. F. BALLOTTA, Arch. di antrop. crim. **47**:688, 1927.

In the first case the injury was caused by a fall on the abdomen from a height of from 3 to 4 meters, resulting in the tear of the first part of the large intestine with peritonitis and death two days later. In the second case, a rupture of the stomach and of the intestine occurred as a result of a fall. Rupture of the alimentary tract is not as rare as is supposed to be by many authors. It does not necessarily require great force. The state of fulness of these viscera is of greater importance in making them less resistent to the effect of injury than their anatomic position.

ACTUAL AND POTENTIAL DAMAGE RESULTING FROM NASAL STENOSIS. LUCA CIURLO, Arch. di antrop. crim. **47**:698, 1927.

The author reviews all possible evil consequences of nasal obstruction. The first effect of impairment of free passage of air is to aggravate the frequently existing chronic and hypertrophic rhinitis resulting in an abundant mucous-mucopurulent and purulent secretion. It also leads to a characteristic nasal facies. Loss of taste, improper phonation, occlusion of the eustachian tube, sinusitis, and impairment of vision are some of the remote effects. It has been demonstrated that an increase in arterial blood pressure and other circulatory disturbances because of diminished aeration of blood takes place. Pressure on the nasal nerve filaments may reflexly give rise to the following morbid phenomena, trigeminal neuralgia, vertigo, epileptic attacks, hemicrania and chorea. Relation of nasal deformities to working capacity is not properly appreciated. Ciurlo urges a larger conception of responsibility on the part of law encompassing all of the potential results of nasal injury to respiratory and circulatory organs, to the senses of smell, hearing, phonation and vision. The potential damage should be estimated on probabilities. He reviews the disability percentages recommended by various authors and proposes a scale of his own which is as follows: complete unilateral obstruction, from 8 to 10 per cent; reduction of permeability of one side to one half, from 5 to 7 per cent; complete bilateral obstruction, from 20 to 25 per cent; bilateral nasal stenosis of second grade, from 10 to 20 per cent; unilateral obstruction with lacrimal duct stenosis, from 18 to 20 per cent; bilateral stenosis with lacrimal duct obstruction, from 35 to 40 per cent, and amosmia of the second degree, from 5 to 10 per cent.

GAS GANGRENE FOLLOWING SUBCUTANEOUS INJECTIONS. W. ANSCHÜTZ, Beitr. z. klin. Chir. **139**:129, 1927.

From gas gangrene caused by *B. welchii*, by the bacillus of malignant edema or by anaerobic strains of *B. coli* in wounds made for subcutaneous injections, twenty-one severe illnesses or deaths are reported. In discussing the report, Batzdorff mentioned sixteen other similar infections after subcutaneous injection of physiologic sodium chloride solution. These are usually phlegmons of the abdominal wall and heal slowly. In the few discovered, the source of infection was the instruments or solutions employed. Cachexia apparently predisposes to gangrene. The opinion is expressed that these occurrences are more common than is indicated by published reports.

E. R. LE COUNT.

GANGRENE OF THE EXTREMITIES FOLLOWING SUBCUTANEOUS INJURIES FROM BLUNT FORCE. H. GREGORA, Beitr. z. klin. Chir. **140**:199, 1927.

Blunt force may crush the soft parts so that gangrene follows, even though the skin is untorn by the injury. This kind of external violence may also tear blood vessels so that gangrene of the extremity develops distally; or they may be torn by bone broken at the same time. The latter mode of development of gangrene of the extremities following subcutaneous injuries in the less common.

Four amputations are reported for gangrene due to subcutaneous lacerations of blood vessels; in three, a popliteal artery and in one, the femoral in the adductor sheath. The popliteal vessels were torn across completely, the femoral partially. All accompanied fractures, but in one patient, the fracture was some distance away from the torn popliteal artery. The torn blood vessels at the dislocated elbow in a fifth patient were repaired with a good result.

E. R. LE COUNT.

NITROBENZENE POISONING. H. SCHNOPFHAGEN, Wien. klin. Wchnschr. **40**:998, 1927.

Following self-attempted abortion by drinking oil of mirbane (nitrobenzene), there was considerable difficulty in deciding clinically to what the poisoning was due. The young woman, aged 20, who was three months' pregnant, soon became unconscious. Stomach washings, the breath and the air of the room where she lay were all redolent with oil of almonds. Her arms and legs were rigid and flexed; the pupillary reflexes were slow and lessened; other reflexes were absent; the pulse was barely preceptible; respirations were superficial, and there was a deep discoloration of the skin to the color of ripe plums, with the lips, nose, fingers and toes almost black.

Finally, blood was withdrawn from a vein and found to be chocolate brown. Nitrobenzene poisoning was suspected. This substance, it will be recalled is sometimes known as artificial oil of bitter almonds. The symptoms were too prolonged for hydrogen cyanide poisoning and the absence of dyspnea and myosis were opposed to morphine poisoning. When she recovered consciousness after about twelve hours, it was learned she had drunk mirbane oil. Death occurred twenty-six hours after the poisoning and three hours after transfusion of 800 cc. of properly selected blood. The fetus and gestation sac were found undisturbed.

E. R. LE COUNT.

Technical

RESULTS OF LIVER FUNCTION TESTS. E. L. SHERRER, Ann. Int. Med. **1**:63, 1927.

Bromsulphthalein possesses distinct advantage over the older dyes, such as phenoltetrachlorphthalein, in the diagnosis of disturbances in the liver. The test is most useful in cases of disease of the liver without marked jaundice.

WALTER M. SIMPSON.

DIRECT NESSLERIZATION OF KJEHLDAHL DIGESTIONS. H. M. CHILES, J. M. Chem. Soc. **50**:217, 1928.

The use of a protective colloid, gum arabic, is suggested to prevent precipitation of the dispersed color colloid in nesslerized ammonia solutions. The addition of this colloid to the standard Folin-Wu nessler reagent permits the direct nesslerization of Kjehldahl digests containing higher concentrations of ammonia and alkali sulphates than has been hitherto practicable.

ARTHUR LOCKE.

THE ESTIMATION OF PLASMA CHLORIDES. A. E. OSTERBERG and E. V. SCHMIDT, J. Lab. & Clin. Med. **13**:172, 1927.

One cubic centimeter of plasma is pipetted into a 125 cc. Erlenmeyer flask and to this is added 10 cc. of 1:3 nitric acid. The nitric acid is added preferably from a burette, slowly and with agitation of the blood plasma, so that a white, flocculent precipitate of the plasma proteins is obtained. If the nitric acid is poured in rapidly a curdy and rather sticky precipitate is formed which may occlude a certain amount of chlorides within the curds. To this suspension is added 5 cc. of N/35.46 silver nitrate solution, and then 1 cc. of a 20 per cent ferric ammonium sulphate solution. The excess silver is back titrated with N/35.46 ammonium or potassium thiocyanate. One cubic centimeter of the silver solution is equivalent to 1 mg. of chloride, or 1.65 mg. of sodium chloride. The end-point is the first trace of color which spreads throughout the whole solution from the point at which the drop strikes while the flask is gently rotated. This color fades within a few seconds.

S. A. LEVINSON.

TEST FOR URIC ACID. E. PITTARELLI, Policlinico **34**:1503, 1927.

Adding to urine four or five drops of a 10 per cent sodium or potassium hydroxide solution, then 0.5 per cent metol (para-aminophenol sulphate) solution and, finally, 1 per cent sodium or potassium persulphate solution, changes the color to brownish yellow if even traces of uric acid are present. It is best to dilute the urine with from fifteen to twenty volumes of water.

THE QUANTITATIVE ESTIMATION OF GLOBULIN IN THE LIQUOR CEREBROSPINALIS. STEFAN VON NÁDOR-NIKITITS, Klin. Wchnschr. **6**:1709, 1927.

The author mentions his turbidity (diaphanometric) method, already described, which is not entirely satisfactory because of difficulties in preparing standards for comparison. Then he resorted to the Esbach sedimentation procedure with ammonium sulphate as precipitant, and devised a tube in which determinations are made with 1.5 cc. of spinal fluid. Certain details of procedure to shorten the time necessary for complete sedimentation of the precipitate should be consulted in the original.

E. F. HIRSCH.

THE DIAGNOSIS OF PREGNANCY BY HORMONE (HYPOPHYSIS) TEST OF THE URINE. S. ASCHHEIM and B. ZONDEK, Klin. Wchnschr. **7**:8, 1928.

The demonstration in 1 to 2 cc. of urine of the hormone of the anterior lobe of the hypophysis may be regarded as diagnostic of pregnancy.

E. F. HIRSCH.

THE INTERPRETATION OF REACTIONS WITH CEREBROSPINAL FLUID OBTAINED BY SUBOCCIPITAL PUNCTURE. ALOIS M. MEMMESHEIMER, München. med. Wchnschr. **74**:1490, 1927.

The interpretation of reactions with cerebrospinal fluid obtained by suboccipital puncture should be based on deviations from normal values consider-

ably less than those usually regarded for the lumbar spinal fluid. Thus, weakly positive Nonne and Pandy reactions suggest disease. Similar weak reactions with the colloidal gold and mastic tests are deviations from the normal. The normal cell content should be about 10/3 instead of 20/3 as with the lumbar spinal fluid.

ARTHUR LOCKE.

DETERMINATION OF GROUP IN HUMAN BLOOD STAINS. E. WITEBSKY, München. med. Wchnschr. **74**:1581, 1927.

Witebsky describes a method by which he was able to demonstrate the specific group characteristic in alcoholic extracts of spots of human blood of group A several months old, also in organs of group A. The method is by complement fixation with a group-specific antiserum. He obtained the antiserum by treating rabbits with human blood of group A or with alcoholic extract of blood in combination with pig serum.

A RAPID MICROMASTIX REACTION. N. MELCZER and O. DAHMEN, München. med. Wchnschr. **74**:1630, 1927.

The details concerning the preparation of solutions, the method of procedure and the interpretation of results should be consulted in the original.

J. D. WILLEMS.

THE WASSERMANN TEST WITH LARGE AMOUNTS OF SERUM. H. FELKE, München. med. Wchnschr. **40**:1702, 1927.

Serum in the amount of 0.4 cc. in the control tube, and 0.1 cc. and 0.4 cc. with the antigen, are used in this method. By using the larger amount of serum a greater number of positive reactions was obtained. A method for preparing a cholesterinized antigen is also given.

R. BRENNWASSER.

RAPID METHOD OF TESTING FOR BLOOD GROUPS. C. E. LIM and K. YAO, China M. J. **41**:513, 1927.

A few drops of blood from the finger or ear are mixed with approximately ten times the amount of citrated salt solution and four or five drops are dried on a clean slide in the air. Two or three drops of salt solution are then added to the slide, which is tilted a few times so that the solution can dissolve the dried serum with as little disturbing of the corpuscles as possible. The same procedure is carried out for both donor and recipient, and a drop of the dissolved serum and a drop of the blood suspension to be tested are mixed on a color glass which is inverted on a hollow slide and left at room temperature for fifteen minutes.

Society Transactions

CHICAGO PATHOLOGICAL SOCIETY

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ESMOND R. LONG, *Vice-President, in the Chair*

STUDIES ON THE SEDIMENTATION REACTION: ITS RELATION TO FIBRIN AND CHOLESTEROL CONTENT OF THE BLOOD AND ITS APPLICATION IN TUBERCULOSIS. MAX PINNER, KATHRYN KNOWLTON and R. GREEN KELLY.

The complete report will be published in the ARCHIVES OF PATHOLOGY.

FULMINANT EPIDEMIC MENINGITIS WITH DEATH IN NINE HOURS. PAUL R. CANNON and ESMOND R. LONG. (From the Department of Pathology, The University of Chicago.)

In fulminant epidemic meningitis many patients die within twenty-four hours, and occasionally, in less than twelve. Our report deals with one in the latter group, and perhaps will throw some light on the pathogenesis of such conditions. A survey of the literature indicates that the earlier death occurs in these instances, the less the symptoms are characteristically meningeal and the more they are the symptoms of a profound toxemia. In recent years, certain studies favor the view that a meningococcus bacteremia precedes meningeal localization. This idea has been particularly advocated by W. W. Herrick (Oxford Medicine, 1927).

The most fulminant illness of which we are aware is reported by Samuel Gordon in the *Dublin Quarterly Journal of Medical Sciences* in May, 1867, in which death occurred four and one-fourth hours after the onset of symptoms, with a course similar to that reported here. The necropsy disclosed an early meningitis.

We record the illness of a girl, aged 4 years and 5 months, under the care of Dr. C. S. Salmon, who first saw the patient at 7 p. m. on June 18, 1927. About noon the child, who seemed well throughout the morning, began to vomit and complained of "stomach-ache" and a severe headache. A week previously she had had a similar attack of abdominal pain, but no other symptoms, from which she recovered and seemed well until the present illness. The child was acutely ill and stuporous; she vomited and had a rectal temperature of 104 F. Rigidity of the neck and Kernig's sign were not noted, but the pupils were dilated. Other abnormalities were not present except a diffuse redness of the tonsils. At 8 p. m., she had convulsions and at 8:30, a marked carpopedal spasm. The pupils were unequal, the right being widely dilated; the skin was dusky and the respiration of the Cheyne-Stokes type, but there was no rigidity of the neck. Diffuse râles were heard in the lungs, and death occurred at 9 p. m. due to respiratory failure, the heart beating for some minutes after respiration stopped.

Necropsy performed at 9:30 the following morning disclosed an early seropurulent meningitis. There were also petechial hemorrhages in the serosa of the small intestine, and larger hemorrhages into the suprarenal glands and pancreas. There was edema of the lungs. The base of the skull was normal. Microscopic examination revealed, in addition, excessive numbers of polymorphonuclear leukocytes in the entire capillary system, an acute focal myocarditis, a mycotic abscess in the cerebellum and multiple microscopic hemorrhages in the cerebrum. On the basis of these observations, the existence of a septicemia was recognized.

Stained preparations of the cerebrospinal fluid revealed many polymorphonuclear leukocytes and gram-negative intracellular and extracellular, biscuit-shaped diplococci. On blood agar, colonies of gram-negative diplococci exhibiting marked pleomorphism developed.

Although blood cultures were not made, the microscopic observations obviously justified the diagnosis of septicemia. The question of the relative age of the septicemic lesions and the meningitis is not so easily settled. The absorption in the areas of acute interstitial myocarditis suggests an older age than nine hours. However, there had not been any symptoms which could be traced to this condition. On the other hand, symptoms of toxemia were pronounced. An interesting point is the relation of the abdominal attack one week previously to the final illness. According to the father, the gastrointestinal symptoms were the same in the two instances. In the meantime, however, she had appeared to be normal. The only lesions of the bowel were the hemorrhagic spots to which particular attention has been called by other observers. In this case as in others reported, it is possible that the hemorrhage into the suprarenal glands may have been responsible for some of the symptoms of collapse.

This case supports the view that the septicemia is as important a factor in the fulminance and early death of these patients as the meningitis, and reemphasizes the desirability of more study directed toward the portal of entry and early development of acute meningococcus infection.

DISCUSSION

I. PILOT: I saw a case in which death occurred in about twelve hours.

METHOD OF REPEATED INTRA-ARTERIAL SYSTOLIC BLOOD PRESSURE DETERMINATIONS IN DOGS. CLYDE R. JENSEN and CARL W. APFELBACH. (From the Pathological Laboratory of the Presbyterian Hospital of Chicago and the Norman Bridge Pathological Laboratory of the Rush Medical College of the University of Chicago.)

An apparatus for making repeated blood pressure determinations in unanesthetized animals was described.

The mercury manometer is a U-shaped tube, with a bore of 1 or 2 mm. in diameter mounted on the front of a rectangular box which is open at the top and back. The side arm connecting with a needle is approximately on a level with the femoral artery of a dog tied to an operating board. At the upper end of the same arm of the U-tube is a stopcock, the latter joining the U-tube with a bottle containing a 2 per cent solution of sodium citrate. This solution is pumped from the bottle into the U-tube above the mercury and out through the needle. A metric scale is mounted on a movable slide along one side of the U-tube.

Comparisons made between two manometers, one with a cannula in the femoral artery, and the other with a 22 gage needle in the same artery indicates that the determinations made with the apparatus described herein are usually from 2 to 4 mm. below those obtained with a cannula.

DEMONSTRATION OF A LITHOPEDION. LOUISA HEMKEN BACON. (From the Norman Bridge Pathological Laboratory of Rush Medical College and the Surgical Service of Daniel Orth of the Columbus Memorial Hospital.)

The interest in lithopedions was at its highest when Küchenmeister (Ueber Lithopedion, *Arch. f. Geb. u. Gynäk.* **17**:153, 1881) published his well known classification in 1881. Since then the subject has become less important because laparotomies are performed as soon as the diagnosis of a ruptured ectopic pregnancy is made.

This report concerns a patient, Mrs. Z., aged 55, who was admitted to the service of Dr. Daniel Orth in the Columbus Memorial Hospital on May 31,

1927, complaining of a mass in the abdomen. She was extremely obese, with an umbilical hernia the size of a lemon, which was easily reducible. Below and to the left of the hernia was a hard, slightly movable mass, the size of a fist. The hernial sac was opened, the omentum freed from its adhesions and a large, hard nodular mass, the size of a grape fruit removed. Its sole attachment was to the right broad ligament. Recovery was uneventful.

It was subsequently ascertained that the patient has seven healthy children and had never miscarried. The menstrual history was normal, and the menopause occurred in 1925.

The formaldehyde hardened lithopedion weighed 549 Gm. a month after removal. It was the shape of a large kidney. It had been partially divided into two symmetrical halves by a longitudinal incision, the longest diameter being 11.3 cm.; the shortest, 8.7 cm.; the maximum circumference, 35 cm. and the minimum, 29 cm.

The lithopedion was of bony consistency with a white glistening peritoneal covering from 1 to 4 cm. thick. Near the upper pole of one side was an embedded femur 7.2 cm. long and 1.5 and 1 cm. wide at the extremities. Above it was a loosely attached phalanx, 15 by 43 mm. Beneath the femur another one was embedded; it was 6 cm. long, 1.4 and 1.2 cm. wide at the extremities, and 5 mm. wide at the shaft. Below this was a region 3 by 1.5 cm., of nine small bony elevations from 2 to 3 mm. in diameter, raised from 1 to 1.5 mm. At the tip of the upper pole was a tag of omental fat 5 by 2 cm. On the other side, underneath the longitudinal incision, was another region with similar elevations.

At the upper pole was a gap, 2.5 cm. wide, from which one of the skull bones protruded for 5 cm. A similar gap at the lower pole had three ribs protruding. Beneath these was 2.5 cm. of the right tube, slightly tortuous, with a minute channel open throughout.

When opened, one half contained the fetal bones (with the exception of the pelvic and long bones) and the thoracic and upper abdominal viscera. The right parietal bone was attached to the outer covering; it was 7 by 6 cm. and 0.05 mm. thick; the inner surface was granular and studded with minute calcareous particles. The remaining inner part of the outer coat was covered with yellow skin, superficial fascia, pale, friable yellow fat and a few muscle strands.

The other half contained the pelvic bones and the large intestine. Its outer covering contained the following bones, all variously placed in relation to each other and all embedded. They were removed. The left humerus was 5.3 cm. long, 4 mm. wide in the shaft, 1.5 cm. at the condyles; the head was missing (later found in left glenoid cavity). The right humerus was like the left. The scapula was 2.2 by 1.8 cm. The two radii and ulnar bones were 4 cm. by 3 mm., and 5 cm. by 3 mm., respectively. The fibulae were 5 cm. long; the tibiae 5.1 cm.

There was no skin on the calvarium. The diameters of the head were: mento-occipital, 9 cm.; fronto-occipital, 10.4 cm.; biparietal, 7.7 cm.; bitemporal, 6 cm.; suboccipito-bregmatic, 8.1 cm. The right side of the face, cut through in the longitudinal incision, had also been compressed by the wall of the chest. The eyes were sunken; the nose and mouth were normal and the ears were absent. The parietal bones overlapped the frontal. There were two sets of frontal bones. The right temporal bone was missing; the left was 1.8 by 1.2 cm. The squamous part of the occipital was firmly embedded in the neck. The dura was normal. The brain was a red-brown mushy mass.

Strands of muscle fibers were in the neck. The umbilical cord was absent because of a transverse incision passing through at this level. The superficial fascia and fat was 5 mm. on the anterior wall of the chest. The pericardial sac and heart was the size of a large strawberry. The right auricle was 15 by 5 mm.; the left 17 by 5 mm.; the mitral leaflets were 2.3 cm. in circumference; the tricuspid 1.8 cm.; the myocardium at the apex was 3 mm. thick; it was beefy red. The aorta was 15 mm. in circumference.

The left lung was 15 by 25 by 4 mm.; the right, 35 by 25 by 5 mm. Both were white and grooved by pressure of the ribs. The surfaces made by sectioning were spongy. The trachea and bronchi were normal. The diaphragm was normal.

The liver, stomach and small and large intestine were the only recognizable abdominal organs. The liver was 3 by 2.3 cm. by 4 mm., and pale green-gray. The stomach was smooth-walled filled with a yellow mucoid material; its capacity was about 10 cc. The small intestine was 7.2 cm. long, 1 cm. in circumference and gray, smooth and glistening. The large bowel consisted of five loops, each 2 cm. long, 1.8 cm. in circumference, the last loop ending blindly in a pouch (rectum). The aorta and its branches were traced down to the inguinal region, the smallest branches ending in the fascia. The renal arteries could not be found.

There was a moderate scoliosis to the left. Eleven ribs were present on each side; the upper five with normal attachments; the lower six attached to the pelvic bones and embedded in the fascia. The ribs were about 5 cm. long. The left scapula had retained its normal position. There were no external genitalia. The ilium was 2 by 2.5 cm.; the ischium was the size of a small hazel nut.

Microscopic Examination.—Sections of the right tube were without noteworthy change. The outer layer of the sac was a vascular dense connective tissue network. Brown fibers were the only remnants of skeletal muscles. Sections of all the viscera consisted of a brown, ill defined staining material.

Küchenmeister divided "stone-children" into three classes. The lithokelyphos in which the placenta calcified about the mummified fetus; the lithokelyphopedion in which the fetus calcifies at its points of adhesions with the placenta and the lithopedion in which the membranes are ruptured and the smegma becomes calcified about the mummified fetus. This author found records of twenty-four lithokelyphoses occurring in women in the thirties who had borne several children; three records of lithokelyphopedion in women with no preceding pregnancies and eighteen records of lithopedion. The shortest time for carrying a stone child was two years, the longest fifty-six years; the average time is twenty-three years.

Extra-uterine pregnancy predisposes to the formation of stone children. Young embryos, between 2 and 3 months of age, are absorbed, as shown by the experiments of Leopold (Experimentelle Untersuchungen über das Schicksal implantirter Föten, *Arch. f. Geb. u. Gynäk.* **18**:53, 1881), who transplanted rabbit embryos of all ages into the abdominal cavity. The youngest were always absorbed. He succeeded in forming one lithokelyphopedion, and in many others found the embryos much changed and a coincident plastic peritonitis.

There is always the grave danger of fatal peritonitis with decomposition and infection of the fetus. This may occur at once after rupture or many years after the lithopedion has formed; the danger decreases as the age of the stone child increases.

Vogt (Das Steinkind von Weissbach, *Arch. f. Geb. u. Gynäk.* **115**:624, 1922) reports sudden cessation of labor pains in a patient whose abdomen decreased in size during the following months. At necropsy many years later, a lithokelyphos was found in the abdominal cavity.

Von Winckel (Ueber die Missbildungen von ektopisch entwickelten Früchten u. deren Ursachen, Wiesbaden, 1902) believes that 10 per cent of ectopic pregnancies have some associated congenital malformation, and that the rupture is a defensive reaction on the part of nature to terminate the pregnancy. The lithopedion is the best protection for the mother, and from statistics of Strauss (Zur Casualistik u. Statistik der Lithopedion, *Arch. f. Geb. u. Gynäk.* **68**:730, 1903), it is the usual outcome. In a series of 7,311 necropsies he found two lithopedions, in another of 610, nine lithopedions.

The symptomatology varies. Occasionally the patient does not suffer from any disturbances; more often there are signs of a large tumor, associated with

a feeling of heaviness, with rupture of the sac and death of the fetus; peritonitis may develop from which the patient slowly recovers. Normal menses reappear. As a rule, conception does not occur again.

FAT REPLACEMENT OF THE KIDNEY IN CHRONIC SUPPURATIVE PYELITIS. LOUISA HEMKEN BACON and E. R. LECOUNT. (From the Norman Bridge Pathological Laboratory of Rush Medical College and the Urological Service of Dr. Vincent O'Conor of the Washington Boulevard Hospital, Chicago).

Replacement of diseased viscera and skeletal muscle with fat sometimes referred to as "Vacat-Wucherung" by German writers is not uncommon. Its occurrence in the kidneys is much more frequent than is indicated by the few references to it in the medical literature. We have found accounts of only sixteen cases, eleven by Godard (Récherches sur la substitution graisseuse de rein, *Compt. rend. Soc. de biol.* **2**:261, 1859), including his own report, and five by other writers (Brown, W.: Fatty Kidney, *Tr. Path. Soc. London* **13**:131, 1861. Rickards, E.: Remarks on the Fatty Transformation of the Kidney, *Brit. M. J.* **2**:2, 1883. Whipham: Case in Which Kidney Transformed Into Fat, *Tr. Path. London* **19**:261, 1867-1868. Heath, C.: Fatty and Atrophied Kidney, ibid. **10**:199, 1858-1859. Ebstein, W.: Nierenkrankheiten, Ziemssen, H. v., Handbuch der speziellen Pathologie und Therapie, 1875, vol. 9, p. 88). The disease is usually unilateral. In only one of the eleven cases assembled by Godard were both kidneys involved. They were so replaced by fat that only a few remnants of renal tissue remained and death resulted from uremia (Rayer, M.: Traité des maladies des reins, Paris, 1841, vol. 3, p. 616). In the kidney studied by Heath, no renal artery, vein or ureter was found, and the other kidney was normal. With this exception, no anomalies have been reported in these adipose kidneys.

A calculus usually obstructs the ureter, and pyelitis, hydronephrosis or renal stone may be demonstrated clinically; or the unilateral disease may not cause any symptoms and be incidental to disease elsewhere responsible for death. The kidney disappears by pressure atrophy in the usual way so that only scattered parts of the cortex remain in the adipose tissue in late stages. These form a shell about a cavity made up of dilated pelvis and calyces. The sac contains pus varying widely in color and consistency. It may be thin and watery or inspissated. It seems more reasonable to regard the invasion of adipose tissue as a compensatory replacement than an ingrowth which causes disappearance of the renal parenchyma. As the medullary pyramids, columns of Bertini and cortex are removed by pressure atrophy, the fat takes their place, growing in and about the blood vessels.

The adipose tissue normally abundant about the kidney usually does not grow through the capsule, although it is continuous at the renal root with that which replaces the kidney. The kidney thus retains its normal shape. In spite of this retained form and size, the adipose tissue is so abundant that there has been a disposition by some observers to regard the condition as lipoma of the kidney. We have not found any explanation by others and have no suggestion to explain the relative rarity of adipose kidneys. Chronic suppurative pyelitis, ureteral obstruction and pressure atrophy more commonly lead to a sacculated kidney considerably larger than the normal kidney than to kidneys about normal size or slightly smaller extensively replaced by adipose tissue. That obesity and good bodily nutrition may contribute to the latter sequence is in some degree controverted by the presence of small kidneys or kidneys of normal size with the parenchyma nearly all destroyed by chronic disease and replaced by fat in markedly emaciated bodies from which the adipose tissue elsewhere has completely or almost completely disappeared.

We examined one of the kidneys removed from a woman, aged 39, in the service of Dr. O'Conor and the late Dr. Lounsbury at the Washington Boulevard Hospital. She did not give a history of kidney disease, but an incompletely filled right renal pelvis with stones was found in a pyelogram and at the level of the sacro-iliac joint the ureter was dilated and slightly tortuous.

In the uncentrifugalized urine from that side, there were 2,000 leukocytes per low power field. The diagnosis of chronic pyelitis and hydronephrosis was made. The kidney was found more adherent than usual at the operation; recovery was uneventful. After remaining in formaldehyde for some time the kidney still weighed 282 Gm. It measured 16 by 6 by 5 cm., with the contour of a normal kidney; the hilum was filled with adipose tissue 6 by 4 by 2 cm.; it was embedded all about the ureter and vessels. The capsule was 5 mm. thick and came away easily uncovering rounded or slightly irregular outpouchings elevated from 1 to 1.5 cm. on both front and back surfaces. Those in front numbered 10 and were from 3.5 by 2 cm. to 10 by 12 mm. in diameter. There were all easily indented. Sectioning of the kidney as usual into front and back halves opened six pouches, all from 3 to 10 mm. from the outer surface and continuous with others of a similar size opening into the dilated pelvis. These were dilated major and minor calyces, the largest being 3.5 by 1 cm.; the smallest, 10 by 5 mm. Three of the smaller sacs contained friable brown calculi. There was no trace of renal pyramids. The fat of the hilum, more exposed by sectioning, was 7 by 6.5 by 2.5 cm. continuous with the perirenal fat and vividly demarcated. The disease was least advanced at the upper pole.

A second kidney (service of Dr. O'Conor) was from a man, aged 54. It was the left kidney, and the clinical diagnosis made was a stone or stones with a stricture of the ureter, for the catheter passed only 10 cm. into the ureter. With the cystoscope pus was seen oozing from that ureter. When the kidney was removed a small abscess was noted in the upper pole communicating with the pelvis. Subsequently this was found to be one of the dilated calyces with total disappearance of the parenchyma at that place.

The kidney was enlarged, 14.5 by 7.6 by 4.5 cm., and weighed 480 Gm. The capsule stripped easily and beneath it were two patches of adipose tissue, one near the upper pole 4 by 3 cm., the other on the dorsal surface 9.5 by 5 cm. Each of these was continuous with the fat about the pelvis and large blood vessels at the root of the kidney.

This fat in the dorsal half of the kidney had replaced most of the parenchyma. In the front half, many of the medullary pyramids were almost entirely replaced by fat. The dilated calyces contained calculi, the largest weighing 59 Gm.

A microscopic examination was made of portions of each kidney after a prolonged treatment with Orth's fluid, pieces then frozen and the sections thus obtained stained for fat with sudan III. At the line of junction of the adipose tissue and remaining renal tissue, we did not find evidence of compression by the fat. The inflammation at such places was no more marked than elsewhere and, in general, the alterations did not differ from those present when pyelophritis and calculi in the renal pelvis are unaccompanied by ingrown adipose tissue. The adipose tissue which had replaced the parenchyma of the kidney resembled normal adipose tissue in all particulars.

MINNESOTA PATHOLOGICAL SOCIETY

Regular Meeting, Jan. 17, 1928

A. H. PEDERSEN, *President, in the Chair*
E. T. BELL, *Secretary*

REPORT OF THREE CASES OF PRIMARY HYPERTENSION AND ASSOCIATED HYPERTHYROIDISM. C. A. MCKINLAY.

Three cases are reported in which hyperthyroidism was associated with primary hypertension. In one patient, a woman aged 39, with primary hypertension, hyperthyroidism associated with adenomatous goiter developed while the patient was under obsevation, and the condition was arrested within a

period of three months by a thyroidectomy. The hypertension continued throughout and was not influenced by the operation.

Two other patients, women, aged 40 and 45, were not seen before the exophthalmic goiter developed. After the symptoms of exophthalmic goiter had been relieved by thyroidectomy and after the basal metabolic rates had returned to normal, the clinical picture was that of primary hypertension with an elevated diastolic pressure above 100 mm. of mercury and with changes in the retinal vessels. Not only has the systolic hypertension of exophthalmic goiter, when present, returned to normal after thyroidectomy in observed cases, but diastolic hypertension has not occurred as a manifestation in exophthalmic goiter. Therefore, it has been presumed that the cases of exophthalmic goiter reported represent a combination of two disease processes, and that the exophthalmic goiter superimposed on primary hypertension accounted for the rapid development of cardiac decompensation through its extra load of work on the heart.

THE AUTOPSY. MARGARET WARWICK.

In spite of the fact that the importance of autopsies is recognized by many authors in medical literature, at the present time autopsies are performed on only about 7 per cent of the persons who die in the United States. The Council of Medical Education and Hospitals of the American Medical Association has ruled that, after Jan. 1, 1928, every hospital to be approved for internship must make an autopsy on at least 10 per cent of the patients who die in the hospital, and after Jan. 1, 1928, the number must be increased to 15 per cent.

The responsibility for making these autopsies must be shared by the hospital superintendent, the pathologist and the clinician. The superintendent must provide a competent pathologist, satisfactory equipment and assistance, as well as pleasant working conditions. He must also be responsible for the interns' instruction in the art of obtaining autopsies and their encouragement toward obtaining as many as possible. The pathologist must be well trained, tactful and deft, and must cooperate with the superintendent, the interns, the clinicians and the undertaker. The clinician should be willing to assist in the obtaining of autopsies, should attend as many as possible, should see that the family of the deceased is notified of the observations, should attend the clinical pathologic conference and contribute to it, should be willing to cooperate with the pathologist in the publishing of reports and papers based on autopsy observations and should be willing to permit an autopsy on himself or his family.

The permission should be requested by the intern on the service, with the help of his superiors when necessary. He should present it as a favor to be extended to the family as part of the courtesy and service offered to the patients in a modern, well equipped hospital. The benefit to the family should be stressed, the value in collecting insurance or compensation, the knowledge of diseases in the family and the satisfaction of knowing the real cause of death. The relatives should be told of the knowledge gained by the intern and physician on the case, the possibility of helping some one else and the contribution to the development of medical science.

The majority of refusals to permit autopsies is due to sentimental objections, the Jewish religion and the activity of undertakers. All of these may be overcome by the education of the general public through cooperation of pathologists, hospital superintendents, clinicians and undertakers.

At the University of Minnesota, the autopsies performed by various members of the Department of Pathology at various hospitals and morgues situated in St. Paul and Minneapolis are grouped together in the departmental files and in 1927 totaled 1,350. In Minneapolis, autopsies were performed on 19 per cent of those who died in that city.

CONGENITAL STENOSIS OF THE CONUS ARTERIOSUS WITH ECTASIA OF THE PULMONARY ARTERY AND BACTERIAL ENDOCARDITIS OF THE PULMONARY VALVE.
L. W. NABERS.

A white woman, aged 48, was admitted to the Asbury Hospital on Nov. 17, 1927, complaining of chills, fever, weakness and drowsiness. The present illness began three months before admission to the hospital, following an attack of a disease diagnosed as "intestinal flu," complicated with severe cystitis. Although very weak, the patient was able to be up after this illness until November 10, when she had a "fainting attack" and since that time she had been confined to bed. For the past week she had had one or two severe chills daily, each followed by a rise in temperature. After the chill she would be extremely drowsy and usually sleep for a long time. She said that she had always had a heart murmur.

The patient had always been healthy. There was no history of rheumatic fever, but she had had frequent attacks of sore throat. In 1907, she had diphtheria which was of more than moderate severity. Her father and mother both died of apoplexy at the age of 57 and 76, respectively.

The results of the physical examination at the time of admission were negative except for a loud systolic murmur heard over the entire precordium, but loudest in the third left intercostal space, immediately adjacent to the sternum. The pulse rate was 92 and the temperature 99.4 F. The blood pressure was: systolic, 84; diastolic, 50.

Blood examination on November 18 showed: hemoglobin (Dare), 100 per cent; red cells, 5,200,000; white cells, 17,500; polymorphonuclears, 55 per cent; lymphocytes, 43 per cent, large mononuclears, 1 per cent, and transitionals, 1 per cent .

Urine examination showed: acid reaction; specific gravity, 1.012; albumin ++ (on basis of four as a maximum); no sugar; 4 or 5 pus cells per low power field and many red blood cells. On November 23, a blood culture gave a pure growth of hemolytic streptococci.

The patient's condition grew steadily worse. Generalized petechiae appeared on December 10, and she died on December 31.

A postmortem examination was made on Jan. 1, 1928. The body was that of a well developed and well nourished white woman, 168 cm. in length and weighing about 140 pounds (63.5 Kg.). There was generalized edema and slight cyanosis of the lips and nail beds. The left pupil was larger than the right and irregular in outline. The left pleural cavity was completely filled with a thin, slightly bile-colored fluid; the right contained 300 cc. of similar fluid. The pericardial sac contained 200 cc. of thin, purulent fluid.

The pulmonary artery was extremely prominent and definitely enlarged near its origin. It measured 10.5 cm. in circumference and showed a saccular aneurysm pointing to the left. When the pulmonary artery was opened, a large, firm thrombus was found which involved two of the cusps as well as the aneurysmal pouch which is adjacent to them. The pulmonary valve was markedly insufficient because of dilatation of the artery at the point of attachment of the leaflets. One of the commissures showed a wide separation of the leaflets. Large thrombotic masses were attached to the leaflets, but old thickening of the leaflets could not be demonstrated. Immediately proximal to the pulmonary ring were two blind pouches, one of which led to the right, the other downward into the wall of the right ventricle. These pouches measured 1 cm. at their mouths and extended for a depth of 2.5 cm. In the conus arteriosus, at a distance of 1.5 cm. from the pulmonary valve, there was marked stenosis; the narrowed portion was 8 mm. in diameter and 1 cm. in length. There was marked hypertrophy of the right ventricle as a result of this stenosis. The heart weighed 450 Gm.

The spleen weighed 200 Gm. There was one small infarct on the posterior surface. The liver, gallbladder, gastro-intestinal tract, pancreas and suprarenals were essentially normal. The left kidney weighed 175 Gm., the right

165 Gm. There were numerous petechial hemorrhages of the pelvis. The uterus was extremely small and of the infantile type; the uterine cavity was practically obliterated. The abdominal aorta showed slightly atheroma. The organs of the head and neck were not examined.

Microscopic examination of the kidney showed a typical diffuse embolic glomerulonephritis. The heart muscle was normal; there were no Aschoff bodies.

Summary.—The condition was therefore a congenital anomaly of the heart, of which the outstanding feature was the stenosis of the conus arteriosus. The pulmonary artery was greatly dilated and the pulmonary valve greatly insufficient because of the dilatation. Because of the stenosis of the conus, the effect was that of a pulmonary stenosis and not that of an insufficiency. The pulmonary valve leaflets showed a bacterial endocarditis which was the immediate cause of death. Bacterial endocarditis is known to be a frequent complication of congenital cardiac disease.

PHILADELPHIA PATHOLOGICAL SOCIETY

Regular Meeting, Feb. 9, 1928

J. Harold Austin, *Presiding*

The Morbid Process in Pernicious Anemia. E. B. Krumbhaar.

Pernicious anemia should still be classified among the hemolytic types of anemia, but not necessarily as primarily due to increased blood destruction. This increased destruction may well be due to the removal of unfit cells, resulting from an antecedent disturbance of the mechanism of hemapoiesis.

In the endeavor to trace the source of this disturbance, the brilliant and constant results of Minot's liver feeding (controlled by observations on the reticulocyte count and bone marrow picture) show that the liver is fundamentally involved. Similar (though unfortunately transient and less constant) results of splenectomy in pernicious anemia indicate that the spleen is also intimately connected. The cessation of progress that this treatment brings to the lesions of the nervous system, glossitis, etc., points toward the elimination of a harmful agent, rather than supplies an item lacking for normal hemapoiesis.

If increased destruction of blood cells and their elimination are considered the fourth and last step in the process, the third might be considered to be bone marrow dyspoiesis, glossitis and nervous lesions, as of the same generation. The second step would then be the disturbance of hepatolienal function (formation of a harmful substance, failure to form a substance necessary for normal function, etc.), which seems to be so successfully relieved by the feeding of the liver. The first step, or primary cause of the disease, may be some of the causative factors already suggested (intestinal toxin or infection, specific parasitic poisons, sequels of partial intestinal obstruction), perhaps all of them or more probably something hitherto totally unsuspected. At all events, it seems preferable today to label diseases of known etiology with a blood picture resembling pernicious anemia as "secondary pernicious anemia." The achylia gastrica—a constant accompaniment—may well be a necessary predisposing cause, and doubtless other predisposing causes (heredity, age, etc.) play their parts.

Bicuspid Aortic Valve. Morris M. Kleinbart.

Two hearts showing bicuspid aortic valves were presented. The first heart was that of a man, aged 50, who died with the clinical diagnosis of gas gangrene of the right leg and right foot. The clinical history did not reveal any symptoms referable to the heart.

At autopsy hypertrophy and dilatation of the heart, chronic mitral endocarditis, bicuspid aortic valve and chronic obliterative pericarditis were found.

The second heart came from a man, aged 39, who died of ulcerative pulmonary tuberculosis. After death hypertrophy and dilatation of the heart and biscuspid aortic valve were found.

Bicuspid aortic valve—a condition in which the normal three cusps of the aortic valve are replaced by two—has long been known to occur as a congenital condition and is commonly regarded as a rare malformation.

Until recently, 169 cases have been reported. Osler reported 18 cases in 1886 and was among the first to call attention to this condition. Lewis and Grant found the condition three times in 215 consecutive autopsies and stated that this probably occurs more often than is found in the literature.

This condition is of clinical interest because of the great tendency for these valves to become the seat of a subacute bacterial inflammatory process and because of the strain on the posterior wall of the aorta, which either ruptures or shows degenerative changes preliminary to the formation of a dissecting aneurysm.

Lewis and Grant stated that 23 per cent of all subjects possessing bicuspid aortic valves acquire infectious endocarditis after reaching adult life. Also, of thirty-one patients seen consecutively, who had subacute bacterial endocarditis, eight, or 26 per cent, presented congenital bicuspid aortic valves.

THE RELATIVE IMPORTANCE OF ENVIRONMENTAL AND INTRACELLULAR FACTORS IN THE BEGINNING OF GROWTH. MAX M. STRUMIA and MORTON MCCUTCHEON.

The experiments reported here were planned as a preliminary attempt to analyze factors influencing growth of cells. It is obvious that all types of growth, whether of individual cells, normal tissues or tumors, are controlled by a variety of factors, some pertaining to the environment and some to the nature and physiologic state of the cells themselves. Thus one can differentiate environmental factors, such as food supply, temperature, hydrogen ion concentration and osmotic pressure, from internal factors such as the age and previous habit of growth of the cell.

The relative importance of these two classes of growth factors, particularly in the case of malignant growths, has been the subject of much speculation and some experimentation. The main difficulty that confronts the investigator is the complexity of conditions when tissues are studied, the difficulty of varying a single factor and measuring a simple reproducible result.

These considerations led Strumia and McCutcheon to analyze growth factors under more simple conditions, with the expectation of later employing the same factors under complex conditions, where, of course, these factors might lead to the same or to different results.

The experiments may be summarized as follows: A certain strain of *Saccharomyces cerevisiae,* adapted to grow in strongly acid medium, was grown for a long time under constant cultural conditions. When transplants were made from growing cultures, subcultures began to grow at once, with an initial rate proportional to the rate at which the parent culture had been growing. When the parent culture had stopped growing, a latent period of several hours elapsed before growth began. The length of this latent period was determined chiefly by the previous history of the culture, in the sense that, when the parent culture had a long latent period, the subculture showed a similar one. In the course of months, this latent period tended to shorten, and then the ability to start growth after a short lag was transmitted to future generations.

Thus it appears that the chief factors regulating the initiation of growth lie in the cell itself, rather than in external conditions. But in addition, changes in the physical surroundings of the culture, especially the osmotic pressure of the medium and temperature, affect the duration of the lag.

In contrast to these factors, the concentration of food in the medium is without effect on the latent period. Even though it greatly affects the shape of the growth curve and the final volume of cells, growth begins at the same time

whether sugar and tomato juice are present in excess or in minimal concentration.

Strumia and McCutcheon were unable to demonstrate that the medium in which cells had been actively growing or in which growth had ceased on account of exhaustion of food contains substances that either shorten or lengthen the latent period; nor by washing the cells was it possible to demonstrate that in making transplants, substances are carried over with the cells that influence the beginning of growth.

PRIMARY NEW GROWTH OF THE PULMONARY ORIFICE. EDWARD WEISS.

G. W., a colored woman, aged 40, was admitted to the Philadelphia General Hospital in the service of Dr. D. J. McCarthy, on Oct. 21, 1927, and died on Nov. 6, 1928.

Her chief complaint, inability to urinate, had come on about three weeks before and a week after the onset was associated with pain during urination. She also suffered from headaches accompanied by vomiting. The past medical history did not reveal anything of importance.

On admission, the woman was well nourished but looked sick and apparently was suffering some pain. Tenderness was present over the bladder region. Laboratory studies did not assist in making the diagnosis. It was thought that the patient had tuberculous meningitis.

At autopsy (C. J. Bucher) there was evidence of acute nephritis. An incidental manifestation was the presence of small nodules at the pulmonic orifice situated behind the pulmonary cusps. At first glance these were thought to be vegetations, but the cusps were free of disease and simply covered these firm, smooth nodules which were attached to the arterial wall at the base of the cusps. Histologic section showed the characteristics of new growth rather than inflammatory tissue. Whether this new growth represented a tumor springing from the muscular coat of the pulmonary artery or was an endothelioma is difficult to say.

PARASITIC CONDITIONS OF THE LUNGS SIMULATING TUBERCULOSIS. DAMASO DE RIVAS.

Of all the diseases common to the respiratory tract, tuberculosis of the lungs probably is the most important; first, because it has been recognized since ancient times as a specific disease and second, because as the etiologic factors of the disease and the pathologic lesions have become better understood in recent years, statistics show that about 60 or 90 per cent of the human race are found to have tuberculosis.

With the exception of few of the rare cases of acute tuberculosis of the lungs in the form of galloping consumption, miliary tuberculosis or the rapid spread of the lesion, tuberculosis commonly is recognized as a chronic condition of no immediate danger to the patient to a great extent, except for the fact that it is a potent predisposing factor to secondary bacterial infection.

The most common symptom of such chronic forms is a dry and persistent cough caused by the mechanical irritation of the lung by the tubercles. In the course of time this irritation may give rise to fibrosis of the lung changing the natural delicate and spongy structure of the organ into a more resistant tissue which in time may eventually produce encapsulation of the tubercles forming what are called "sterile tubercles" or a type of diffuse fibroid phthisis.

Under less favorable conditions, however, the tubercular lesion may spread to the surrounding tissue and give rise to scattered areas of bronchopneumonia with subsequent breaking down of the tissue. As these areas are more or less in the proximity of the bronchioles they may eventually establish connection with the outside, forming what is called "open lesions." These lesions are the source of secondary bacterial infection and formation of abscesses, rapid destruction of the lung tissue giving rise to the formation of cavities, septicemias and a fatal termination.

The foregoing common type of tuberculosis of the lung is too well known to need any detailed description; it is mentioned here merely because of the fact that more or less similar lesions are also reproduced by parasitic conditions of the lung, of which paragonimiasis is the best known.

It may be mentioned in this connection, however, that the parasitic conditions of the lungs are more common than is usually conceded; their number will be found to be still greater if one considers the transitory passage through the lung of the embryonic or larval stage of a great number of parasites which at this stage of their development enter the blood and necessarily pass through the lung previous to reaching their destination. Microfilaria, the larval stage of hookworm and *Ascaris,* in particular, are only a few of the parasitic conditions which may predispose to pneumonia. *Taenia echinococcus,* as is known, gives rise to hydatid cysts simulating tubercles. This enables one to appreciate the fact that among the parasitic conditions as a whole, those of the lungs are second in importance only to those of the alimentary tract which, as is known, constitute about two thirds of all parasitic conditions of man.

In this brief contribution only three, perhaps the most important, parasitic conditions of the lungs are considered, namely, paragonimiasis, schistosomiasis and blastomycosis.

Paragonimiasis.—The adult parasite *Paragonimus westermanii* lives in a semi-encysted condition in the bronchioles of the lungs surrounded by an area of bronchopneumonia. The chief symptom of the condition is a dry cough, which is more or less persistent and is accompanied with hemophthisis. Like tuberculosis, in time these localized bronchopneumonic areas may gradually extend to the surrounding tissue and give rise to softening and degeneration of the lung. By establishing connection with the bronchus, this condition predisposes to secondary bacterial infection, formation of abscesses, suppuration and destruction of the lung tissue, and in all respects, it simulates clinically an open lesion of tuberculosis.

In paragonimiasis, therefore, one finds a condition which clinically cannot be differentiated from tuberculosis, and the differential diagnosis naturally is based on the finding of the eggs of the parasite in the sputum.

Schistosomiasis.—This condition is caused by a trematode of which three species are known as parasites of man, namely, *S. hematobium, S. mansoni* and *S. japonicum.* The adult parasite inhabits the inferior vena cava, the superior and inferior mesenteric vein and the arterioles and hemorrhoidal plexus of the pelvis. *S. hematobium* lives with preference in the blood vessels of the bladder, while *S. mansoni* and *japonicum* are found in the vessels of the rectum. As may be seen, these parasites do not live in the lungs in the adult stage, however, as the eggs of the female are discharged in the circulating blood and carried to the heart, eventually becoming lodged in the lung, this organ acting as a filter. The deposition of eggs is a source of irritation which eventually gives rise to the formation of tubercles and localized areas of bronchopneumonia and often, as is the case in tuberculosis, may eventually lead to softening of the lung tissue, secondary bacterial infection and formation of abscesses.

Blastomycosis.—Blastomycosis is a well known condition of the lung, of which aspergillosis and actinomycosis are best known. Primarily, this condition is localized in the form of tubercles surrounded by bronchopneumonic areas but eventually, as is the case with tuberculosis, they may give rise to softening of the lesion, secondary bacterial infection and formation of abscesses.

General Considerations.—It may be seen by the foregoing brief description that besides pneumonias, tuberculosis and other well known bacterial infections of the lung, there are also a number of parasitic diseases of this organ which, though in many of their respects they may resemble tuberculosis, both clinically and pathologically, are caused by metazoan or vegetable parasites. These facts strongly suggest that in conditions of the lungs simulating tuberculosis, especially in those doubtful cases in which the presence of the tubercle bacillus is not demonstrable in the sputum, a thorough search for the possible presence

of the eggs or larva of some kind of metazoan parasite, or the vegetative form or spore form of fungi or some type of protozoan parasites should receive proper consideration as a routine procedure in the examination of the sputum for a better interpretation of the etiology, symptomatology, treatment and prophylaxis of chronic conditions of the lungs.

NEW YORK PATHOLOGICAL SOCIETY

Regular Meeting, Feb. 9, 1928

HARRISON MARTLAND, *President, in the Chair*

OXYGEN UNSATURATION OF VENOUS BLOOD IN CARDIAC FAILURE. HERBERT W. SCHMITZ and JOHN A. KILLIAN. (From the Department of the Laboratories, New York Post-Graduate Medical School and Hospital.)

This is an abstract of a report on the oxygen unsaturation in patients with severely damaged hearts. The ultimate purpose of the investigation is to determine the relationship between the oxygen unsaturation of the venous arm blood and the clinical symptoms associated with heart failure. In 1918, Lundsgaard (*J. Exper. Med.* **27**:179, 1918), found the unsaturation in twelve patients with compensated heart lesions within normal limits, between 2.5 and 8 per cent by volume. Four patients with uncompensated heart disease showed values above the upper normal limit, from 9.7 to 15.2 per cent by volume. In a case of mitral insufficiency and auricular fibrillation, in which the heart was fully compensated while at rest, the values for the oxygen unsaturation were above the high normal.

Oxygen determinations (oxygen capacity and content) have been made in eleven cases of organic heart disease representing different types of lesions and different degrees of congestive heart failure. The oxygen unsaturation is the difference between the oxygen capacity and the oxygen content. Simultaneous estimations of the carbon dioxide, sugar and lactic acid content were also made. The blood was drawn from a cubital vein without stasis and collected in a 10 cc. syringe under oil. The blood was then transferred under oil into a bottle containing a film of oxalate. The oxygen determinations were made by Van Slyke's manometric method and the lactic acid by the Brehme and Brahdy method.

With one exception, the patients in all the cases studied were bedridden and presented symptoms of congestive failure. Some were and some were not free from dsypnea while at rest at the time the blood determinations were made. The ambulatory or control case was a case of auricular fibrillation, that did not present any symptoms of failure while at rest. This patient gave normal values for the oxygen unsaturation. Three patients, who had had severe congestive failure (class 3) but who had improved so as to be free from dyspnea while at rest, presented normal figures for the oxygen unsaturation. The patient in a case of sphilitic aortitis, arteriosclerosis and chronic nephritis did not have symptoms of heart failure, but had an oxygen unsaturation of 4.4 per cent by volume. The remaining six patients showed values above 8 per cent by volume for the oxygen unsaturation. The values ranged between 8.6 and 15.2. Four of these cases presented symptoms of marked congestive failure, the other two were patients with auricular fibrillation, but without dyspnea while at rest. In the four cases repeated determinations were made. With an improvement in the clinical condition, a decrease in the oxygen unsaturation was noted. One patient showed a marked increase in oxygen unsaturation several hours before death. Another patient, however, with marked failure and congestion and right-sided hydrothorax with a small volume of fluid showed a value of 9 per cent by volume for the oxygen unsaturation, a value slightly higher than the upper normal. Ten days later, after definite

clinical improvement was noted, the oxygen unsaturation dropped to 3.5 per cent by volume. About one month later his condition grew worse, more fluid accumulated in the right chest and orthopnea developed. With the increase in the severity of the symptoms, a rise in the oxygen unsaturation was observed.

In the majority of the cases presenting high values for the oxygen unsaturation, the patients also showed definite increases in the blood lactic acid content. The normal values for the lactic acid content of the blood are assumed to be from 15 to 20 mg. per hundred cubic centimeters of whole blood. In most instances the lactic acid increased as the heart failure became marked. The oxygen unsaturation and the lactic acid increased and decreased coincidently as the severity of the symptoms.

The patient with syphilitic aortitis, arteriosclerosis and chronic nephritis showed a lactic acid content of 30.9 mg. which increased to 34 mg. one week later, but the oxygen unsaturation always remained below the average normal, from 4.4 to 4.6 per cent by volume. In this case, however, the patient did not have any symptoms of heart failure while in bed, and the increase in lactic acid was, probably, the result of the renal lesion.

In one case with severe failure, marked dsypnea and cyanosis, a carbon dioxide content of 41.5 per cent by volume was observed. This is somewhat below the low normal, and was caused, possibly, by the increased pulmonary ventilation.

The effect of exercise, or work, on the oxygen unsaturation was studied in a patient with rheumatic heart disease with fibrillation, who did not present signs of failure while at rest but who showed marked dyspnea on exertion. The exercise consisted of climbing 30 feet of stairs in forty seconds. A control specimen was taken after the patient had rested for thirty minutes. A second specimen was taken within the first minute after the exercise was completed and a third specimen approximately three minutes after the exercise. The oxygen unsaturation of the control specimen was 5.8 per cent by volume, or well within the average normal limit. The oxygen unsaturation of the second specimen was markedly increased, being 15.5 per cent by volume, or about 10 volumes higher. In the third specimen, the oxygen unsaturation had dropped to 9.5. It was observed that the marked increase in the oxygen unsaturation immediately after exercise was mainly due to the increase in the oxygen capacity which had risen from 16 to 24.5 per cent by volume. The value for the oxygen content in the second specimen was only slightly lower than that in the control specimen. This indicates that an increase in the oxygen unsaturation may occur after exertion in patients with heart disease, and that the increase in this value may be due to a rise in the oxygen capacity.

DISCUSSION

HARRISON MARTLAND: Has the work been extended to cardiorenal diseases? Are you not trying to show the presence or absence of anoxemia by chemical methods in order to be able clinically to recognize anoxemia, classify its causes and suggest therapeutic measures? If this is so, it is of great clinical importance. It seems to me it would be interesting to study certain types of hypertensive cardiovascular disease associated with polycythemia and increased viscosity of the blood when the erythropoietic centers are stimulated to form an increased number of red blood cells.

LOUIS GROSS: The speaker mentioned that in some cases, following exercise the oxygen capacity of the blood is increased, and it was suggested that possibly removal of fluid from the blood into the tissues may have been responsible for it. Were any measurements made of the proportion of the red blood cells and the fluid elements of the blood to check up this question?

JOHN A. KILLIAN: These experiments on the effect of exercise on the relation of oxygen capacity of the blood and the volume of red cells to the plasma, or the total solids to the plasma, have not been determined in this study, but they have been in previous experiments, in which we have found

a rise in blood cells compared to the plasma, and also an increase in the viscosity of the blood, which would tend to suggest that the volume of blood is decreased.

THE VERNES FLOCCULATION TEST FOR TUBERCULOSIS: RESULTS OF TWO HUNDRED AND FIFTY CASES. ADELAIDE B. BAYLIS. (From the Department of the Laboratories, New York Post-Graduate Medical School and Hospital and the Department of Medicine, Columbia University.)

The results of two hundred and fifty cases in which the patients were tested by the Vernes technic (*Am. Rev. Tuberc.* **15**:500 [April] 1927) are given. The persons examined included normal controls, and patients with definitely active tuberculosis, as well as examples of several other diseases without and with concomitant tuberculosis. These are reported in detail with a discussion of certain cases. The Vernes test is not specific in a bacteriologic sense, but it is a help in the differential diagnosis of obscure clinical conditions when tuberculosis has to be considered. It is especially helpful as an indicator of arrest or progressive activity of the disease process in the known tuberculous patient.

DISCUSSION

FLORENCE SABIN: It is interesting to see that the flocculation test checks with another technic which possibly indicates the same sort of thing. We are convinced in our experimental work on rabbits that the ratio of monocytes to lymphocytes gives one a chance to follow the lesions and note whether they are quiescent, advancing or receding. That work, at first presented from the experimental side, is now being confirmed in clinical cases, and the last report is that by Morriss and Tan. They have followed the monocyte-lymphocyte ratio in a series of 200 cases. When the lesions were entirely quiescent and the clinical condition unchanged, they were not able to detect any difference between the ratio and the normal, but whenever the lesions were changing, they found the same correlation with the monocyte-lymphocyte ratio that can be demonstrated experimentally in animals. In the chart that Miss Baylis showed, the ratio was gradually declining — an indication that the lesions were gradually decreasing.

WARD J. MACNEAL: I followed the work of Miss Baylis with tremendous interest. It appeals to me as being something valuable. I believe that the conclusions drawn by Miss Baylis are justified by the work.

MULTIPLE NECROSES OF THE SPLEEN WITH SPECIAL REFERENCE TO THE SO-CALLED "SPECKLED SPLEEN" OF FEITIS. KIYOSHI HOSOI. (From the Department of the Laboratories, New York Post-Graduate Medical School and Hospital.)

This paper will be published in full in a later issue of the ARCHIVES OF PATHOLOGY.

DISCUSSION

WARD J. MACNEAL: I have had the opportunity to follow Dr. Hosoi's work. I am inclined to think that when more attention is paid to this condition of the spleen, it will not be so rare as one might judge from the small number of cases reported. Up to date no one has recognized anything during life which is related to this condition; hence it will be overlooked unless sought for post mortem.

I think it is worthy of further emphasis that the "speckled spleen" is not a single entity. At least three varieties of the condition can be recognized. The Fleckmilz of Feitis would appear to occur in persons with advanced disease of the blood vessels, arteriosclerosis and hypertension. Apparently in such cases, sclerosis of the splenic vessels in a predominant factor. It may be that the final result is brought about by some acute toxic condition. There is a second group in which arteriosclerosis, hypertension and evidence of cardio-

vascular disease is lacking, and this type of splenic lesion is associated with marked intoxication, usually acute infectious disease. There are some instances in a third group which do not correspond to either of these, namely, in pernicious anemia. In these, death has followed a transfusion in which there has been a pronounced reaction. One gets the impression that the foreign blood corpuscles have been clumped and have served to initiate this focal necrosis of the spleen by plugging of the terminal vessels in the marginal zone about the splenic follicle. I believe these three varieties can be recognized already, and still other varieties may be recognized. I believe that Dr. Hosoi would not desire to give the impression that speckled spleen is a pathologic entity, but it is a condition possibly produced by a variety of factors.

ALFRED PLAUT: Concerning Dr. MacNeal's remark about the possibility of this condition not being so rare, I would like to state that this lesion was never found in 10,000 autopsies in which I am certain that the spleen was carefully examined. These autopsies included material from a large hospital, more than 2,000 beds, during the last epidemic of influenza. I think this lesion must be not only seldom recognized, but seldom present.

HARRISON MARTLAND: I am sure the lesion is unusual. I have not seen or recognized it in about 6,000 autopsies.

MALIGNANT THYMOMA: REPORT OF A CASE. LOUISE H. MEEKER. (From the Department of the Laboratories, New York Post-Graduate Medical School and Hospital.)

Tumors of the thymus are rare. In the files of the New York Post-Graduate Medical School and Hospital the first record of thymoma was made in June, 1926. This occurred in a woman, aged 33 years. There was a tumor mass in the mediastinum, as shown by roentgenograms, and the cervical lymph nodes were involved. Diagnosis was made from biopsy tissue taken from the cervical lymph nodes. This patient was transferred to another hospital. A second case was recognized in May, 1927. The patient was a man, aged 61, presenting a cystic tumor located below his left ear. This measured 6 by 4 cm. and involved the external auditory meatus. A diagnosis was made of branchial cyst with aberrant thymus containing Hassal's corpuscles in its walls.

The third case is the subject of this report. A woman, aged 23, consulted her surgeon on Aug. 18, 1927. She complained of a swelling in the thyroid region that had existed for six weeks. She was easily tired and had a rapid pulse rate. Physical examination disclosed a lobulated swelling in the thyroid region. Percussion elicited substernal dulness to the base of the heart. A roentgenogram revealed a much enlarged thymus, which was shaped like a pyramid with the base over the heart. The basal metabolism was normal, and the blood picture was normal. At this time, a diagnosis was made of status thymicolymphaticus. The patient was treated with roentgen ray and discharged considerably improved. She was readmitted at the end of three weeks, on September 28. She now complained of enlarged cervical nodes which had suddenly appeared on the left side and were increasing in size. Roentgenograms disclosed a further growth in the mediastinum extending to the left central lung and to the right base, especially pleural thickening, both interlobular and basal, on both the right and the left side. There was an exudate in the right pleural cavity at the base. The blood picture remained normal. A diagnosis of marked mediastinitis, low grade bronchial pneumonia, pleurisy without effusion and enlargement of the thyroid was made. Biopsy tissue taken from the supraclavicular glands was diagnosed "thymoma." The patient was now coughing a good deal, complaining of shortness of breath and of radiating pains throughout the thorax. One thousand three hundred cubic centimeters of fluid, drawn from the right pleural cavity, was negative for cells with mitotic figures. Roentgen-ray treatments were continued, but the hopelessness of the

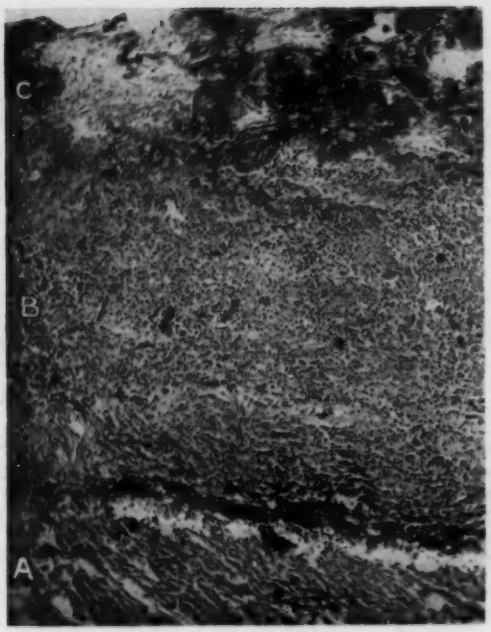

Fig. 1.—Extension of the thymoma into the pericardium. *A* shows the muscle of the heart; *B*, the typical thymic tumor and *C*, necrosis. Low power magnification.

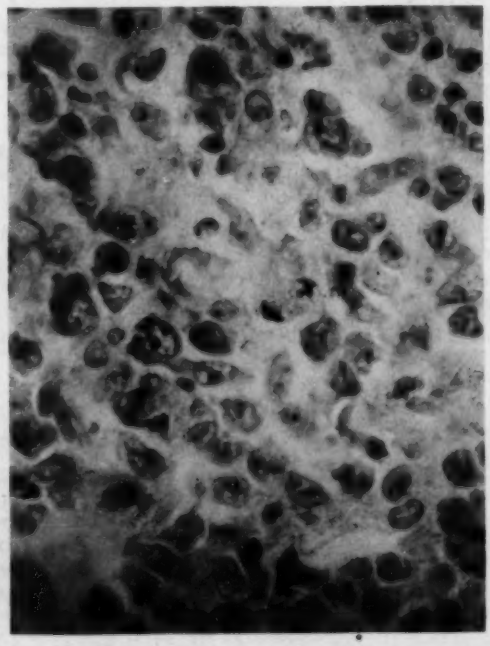

Fig. 2.—Photomicrograph of typical area of thymoma (biopsy tissue). The polyhedral cells, vesicular nuclei with nucleoli, mitosis and phagocytosis should be noted.

case was explained to the family, and the patient was discharged. Death occurred on November 20, and the body was brought to the hospital for examination. The duration of the disease was from July 1 to November 20, about five months. Necropsy was performed twenty-four hours postmortem. The anatomic diagnosis was thymoma with widespread extension metastases.

Grossly, the tumor was white and leathery and had no sharp boundaries. It filled the entire mediastinum extending upward about the larynx, displacing the thyroid, ensheathing the large vessels of the neck and invading the cervical lymph nodes. Its lateral and downward extensions were directly along the pleura and pericardium following the vena cava and prevertebral connective tissue below the diaphragm and spreading to the viscera of the abdomen and pelvis. The abdominal and pelvic localizations included both kidneys, the stomach, intestine and ovary. Extension of thymoma below the diaphragm is rare, and none of the previously reported cases of thymoma has shown the widespread metastasis that has occurred in this case.

Microscopically, the cells forming the tumor were of one general type growing diffusely throughout a scanty stroma, although in some areas the stroma might be abundant. They were rather small cells in part with vesicular nuclei having one nucleolus and with scanty slightly basophilic cytoplasm, although the cytoplasm was acidophilic with some stains. Closely intermingled with these cells there were large cells also with vesicular nuclei having nucleoli and more abundant and paler cytoplasm, often with from one to several protoplasmic processes. Many of the cells, both large and small, contained acidophil granules; still others were phagocytic, and mitotic figures were occasionally fairly numerous and pyknotic forms were common. We have interpreted the tumor cells as more or less closely resembling the so-called thymic cell and the thymic reticular elements. Hassal's corpuscles were found in the new growth.

The first biopsy tissue was taken from the lymph glands of the neck. This showed extensive necrosis and complete loss of normal structure with reticular hyperplasia, and with many plasma and eosinophil cells. The abundant mitotic figures pointed to replacement of the tissue of the gland by tumor cells. This picture resembled with striking accuracy the thymic-tissue metamorphosis after radiation described by Dautchakoff. At no point in the later tumor growth was this so clearly seen.

The second biopsy tissue was a gland from the supraclavicular fossa removed some time after more thorough radiation treatment. Its structure was identical with that of the viable portions of the tumor masses found at autopsy.

Summary.—This tumor filled the requirements for thymoma.

1. It arose in the thymic region.
2. The pleura and pericardium were involved by direct extension.
3. The widespread metastases below the diaphragm were exceptional.
4. There was a general resemblance of the type cells to those of the embryonic or postembryonic thymus.

RETROPERITONEAL LIPOMYXOSARCOMA. NICHOLAS M. ALTER. (From the Department of the Laboratories, New York Post-Graduate Medical School and Hospital.)

A great variety of names have been applied to these tumors which Virchow called "myxoma lipomatodes." In them the yellowish fatlike and the gray gelatinous tissue are the conspicuous features. In this study, the following points have been kept in mind: (1) the histologic nature of these neoplasms with a view to correct classification; (2) the possible transformation of a relatively benign type to a more malignant one and (3) the histogenesis of embryonic fat cells.

CASE 1.—A woman, white, aged 47, entered the hospital with the chief complaint of "swelling of abdomen." The clinical diagnosis was ovarian cyst. At the operation a firm growth was found retroperitoneally embracing the right kidney anteriorly. It had to be detached from the capsule of the kidney and the fascia of the posterior abdominal wall. The growth raised the peritoneum in front, pushing the mesocolon and colon toward the midline. In the removal cleavage was found all around the growth except for the attachment to the capsule of the kidney and posterior fascia. The kidney, of normal appearance, was left behind.

The pathologic report was as follows: The specimen consisted of a large ovoid growth, 28 by 21 by 13 cm. weighing 3,120 Gm. It was well encapsulated. The capsule was rather thick, fibrous and covered with some fibrous tags. On cross-section translucent gray tissue was seen throughout. It had a watery, edematous appearance. There were yellow areas of opaque necrosis. Portions of hemorrhage were also numerous; however, they did not exceed 1 cm. Irregular islands of yellow fatlike tissue were seen scattered throughout the growth and mixed with the other tissues. As a result of this some portions of the growths were yellower and softer, others were grayer and firmer. The capsule and the periphery of the growth were well supplied by blood vessels.

Microscopic sections from various portions of the growth showed a great variety of histologic pictures. In some areas embryonic fatty tissue, and in others fibroblastic proliferation, was seen. There was a meshwork of fine fibrils which were irregular in their course. The fibrils did not stain by the Van Gieson method but became evident with the silver staining. In frozen sections the meshes were filled out by polyhedral cells with acidophilic, finely granular protoplasm. The fine granules stained well with sudan III or osmic acid, and evidently consisted of neutral fat. The protoplasm was irregularly outlined and continued into fine processes. In paraffin sections these cells were collapsed and slender. There were a great many blood vessels with thick walls. There were a few giant cells which reminded one of the foreign body type. Stains for mucin were negative.

The patient was readmitted eighteen months later with the chief complaint of "recurrent swelling of abdomen." During the operation the growth was found in its former bed, but at this time the kidney and a large portion of the posterior fascia had to be removed. The capsule of the kidney was practically inseparable. The growth extended to the pancreas and pushed the mesocolon and the colon to midline. It showed strong attachment to the hilum of the kidney.

The pathologic report was as follows: The specimen consisted of a large, lobulated tumor mass. The posterior surface was covered with a ragged membrane. In its center a kidney was embedded which measured 8 by 4.5 by 3 cm. Between the hilum of the kidney and tumor mass cleavage was not seen. The parenchyma of the kidney was free. The entire mass weighed 5,300 Gm. The tumor measured 37 by 25 by 8 cm. Anteriorly the capsule was uniformly thin and smooth, covering all the lobules. On section, irregular, yellow opaque areas of necrosis and hemorrhage were seen. There was practically no portion that reminded one of mature yellow fatty tissue. The conspicuous color was the reddish gray.

Microscopically the general texture of the recurrent tumor was the same as in the original tumor, but there were certain differences. Giant cells were conspicuously numerous. Some of them were the result of multipolar nuclear divisions. Others reminded one of the foreign body type. The protoplasm of these giant cells consisted of a finely granular mass with vague outlines. The granules stained well with Sudan III or osmic acid. Essentially the growth was made up of lipoblasts, as seen in the original tumor.

The patient has remained well to date.

CASE 2.—A white woman, aged 50, was admitted to the hospital with the chief complaint of "swelling and pain in the right upper abdominal quadrant." At operation a retroperitoneal mass was found in the front of the right kidney.

There was free cleavage around it. The lobulated mass was encapsulated, did not show attachment to any organs and pushed the ascending colon to midline.

The pathologic report was as follows: The specimen consisted of an encapsulated tumor mass of coarsely lobulated structure, 28 by 16 by 14 cm., weighing 2,380 Gm. This mass, when incised, bulged noticeably and presented a translucent cut surface of gelatinous appearance excepting when discolored by hemorrage or mottled by yellow opaque necrosis. The color otherwise varied from a pale bluish to a pinkish gray. It did not grease the knife notably nor drip fluid.

Microscopically, in the hematoxylin-eosin stained section a diffuse growth of stellate cells was seen. In frozen sections their protoplasm appeared to be larger and of finely granular nature. Sudan III was taken up by these granules which also filled the processes. All outlines were vague; large fat globules were at times seen outside these cells. The nuclei, when resting, were centrally placed, small, dark stained. Most of the nuclei, however, were irregular without infrequent mitoses. There were a few giant cells. The intercellular spaces were filled with a granular mass. With hematoxylin-eosin stain a denser stroma was also observed around the well developed blood vessels; this stroma stained red with Van Gieson's method.

Summary.—In both cases reported the patients were women of about the same age, one aged 49, the other aged 50. Both presented similar clinical aspects produced by a rightsided abdominal mass which did not show any particular relationship to the abdominal organs and which pushed the ascending colon to midline. During operation in the first case, the growth appeared to be attached to the capsule of the kidney, but the kidney, of normal appearance, was left. Within eighteen months the growth recurred, reaching a larger size at a rapid rate. At the second operation, the attachment to the capsule of the kidney was marked, and the kidney had to be removed with the mass.

In the second case the encapsulated mass had a free cleavage around it.

On section of all three specimens, the growth appeared to be diffuse. Irregular areas of necrosis and hemorrhage were observed in all three. The color varied; some yellow was seen in the original of the first case, but in all three the gray was conspicuous. There was marked translucence and gelatinous consistency. Microscopically, the predominant cell type was the lipoblast not only in the form of the well known embryonal fat with the signet-ring cells but in the form of cells which were not unlike fibroblasts in the paraffin sections. Frozen sections showed a polygonal cell of considerable anaplasia, particularly in the recurrence, with numerous single and multipolar mitoses. Owing to this nuclear division, lipoblastic giant cells were produced. For the histogenetic explanation the work of Symmers and Fraser is most acceptable. Fatty tumors are often derived from private fat cells set apart in embryonal life. Such primitive fat organs normally exist around the kidneys. Although other tissue elements of mesoblastic origin may occur, the lipoblast is the dominant factor of this type of neoplasm; therefore the appropriate name for both tumors reported is "malignant lipoblastoma."

DISCUSSION

HARRISON MARTLAND: Yesterday I performed an autopsy on a woman who showed a similar condition to that in the case presented by Dr. Alter. I thought I would discuss his paper by showing the specimens from this case which presents certain interesting and unusual features.

These specimens come from an Italian woman, aged 35, the mother of ten children. Two years ago she was delivered of a normal full term child. One year ago she was operated on for the removal of a tumor the size of an orange which was situated in the fat of the left buttock. Microscopic examination showed a liposarcoma. She did well and went home, but complained afterward of severe pain in the pelvis. About four months before death she was admitted to the City Hospital with a tumor mass in the pelvis which was giving her

severe pain. She had had amenorrhea for the last five months. The question of pregnancy or of a tumor came up. Exploratory laparotomy showed a pregnant uterus of five months' size, pushed forward and to the right by a large tumor in the pelvis, which was considered an inoperable sarcoma. The incision was closed without biopsy. After operation the patient returned to her home and had a great deal of pain in her pelvis which was unrelieved by the administration of morphine. Aside from this pain, the pregnancy progressed in a normal manner. She was readmitted to the City Hospital the day before yesterday in labor. Examination showed that delivery was impossible, owing to the presence of a tumor filling the pelvic cavity. A cesarean section was performed, and death followed a short time later. At autopsy a large circumscribed lobulated tumor measuring 8 inches in diameter was found entirely filling the pelvis, making delivery impossible. On section, it was found to be encephaloid and displayed a variety of colors. In places one will observe that it is translucent and pale yellow. In other portions it is a deep orange and translucent. The greater part of the tumor, however, is grayish and granular and reflects high lights. Except for firm adhesions to the left lateral wall of the pelvis, there is no indication of infiltration into the surrounding structures. Situated in the retroperitoneal fat over the left kidney, but in no way connected with its capsule, is a similar growth 6 inches in diameter. It is circumscribed, lobulated and on section shows a similar display of colors. There is a similar growth 3 inches in size in the mesentery of the small intestine. In the retroperitoneal fat behind the lower pole of the right kidney there is another tumor of a similar nature from 2 to 4 inches in size. Located in the fat of the gastrocolic omentum, in the lesser sac and near these other tumors, are some twenty smaller tumors, fatty in nature, ranging from 0.25 to 1 inch in size. They are circumscribed, often pedunculated and the larger ones are slightly lobulated. On section they are yellow and translucent. Frozen sections show the smaller tumors to be lipomas in which the predominant cell is a fat cell of the adult type. Embryonal fat cells containing a smaller amount of fat can be seen in some areas. In some areas which are a deep orange the cells contain a granular lipoid pigment resembling xanthoma cells. In the large tumors, many portions show transition into liposarcoma or lipomyxosarcoma. Here the cells are polyhedral, contain little fat and are often arranged in alveolar fashion. Tumor mitosis and hyperchromatism are occasionally seen in these cellular areas. There is no recurrence in loco of the growth removed at operation from the buttocks. There are no other subcutaneous tumors. There are no metastases to the lungs and no involvement of the lymph nodes in any part of the body. There is no involvement of any other fat tissue than that already described. In this case we seem to have a condition of multiple benign lipomas, confined to the retroperitoneal fat tissues and the abdominal and subcutaneous fat of the buttock. A transition of many of the tumors into liposarcoma has occurred at one or more periods of time. It is extremely difficult to interpret any of these tumors as being metastatic in origin. Dr. Alter has covered the subject of retroperitoneal lipoma so thoroughly that little can be added.

Book Reviews

THE RISE AND FALL OF DISEASE IN ILLINOIS. By ISAAC D. RAWLINGS, M.S., M.D., in collaboration with WILLIAM A. EVANS, M.D., D.P.H.; GOTTFRIED KOEHLER, M.D., and BAXTER K. RICHARDSON, A.B. Published by The State Department of Public Health in commemoration of its fiftieth anniversary, 1927. Illustrated with graphs developed and drawn by A. F. Dappert, and with picture reproductions of many persons associated in one way or another with the story. Indexed by Clara Breen. In two parts.

This volume on the history of health and disease in Illinois is an extended treatise written largely so that "he who runs may read." It sets an example which it is to be hoped health departments in other states and other official and unofficial agencies will follow. The American public needs education on the history of hygiene and sanitation that it may take a more general and a more soundly based interest in health problems. The authors are to be congratulated on an important contribution. May it be anticipated, however, that subsequent books of the same kind will be free from the shortcomings of this one.

The story of disease in Illinois is divided into two parts. The first part deals with the history from the earliest days to 1877 — the year of the establishment of the state's department of health; and the second, with the story since 1877. The general history and the history of certain diseases prior to 1877 are largely superficial and casual. In a measure this is unavoidable because the official and scholarly records are scanty. But in another measure — larger or smaller — the superficiality rests with the treatment. In the second part, the development of the state health machinery is presented adequately and thoroughly. It is to be regretted that an equivalent treatment was not accorded discussions of incidence of morbidity and mortality since 1877. For some diseases at least, and for parts of the state certainly, detailed official records are available. Some of them are presented. But the faults lie in the discussion accorded them. No one will quarrel with the picture that is presented for the occasional rise and the more regular fall of disease in Illinois. The story of the partial or complete conquest of many diseases is plain enough. It is written in the general and economic history of a great state, and more indelibly in the elimination or control of many causes of death. There can be little doubt that the general death rate has fallen from something of the order of twenty (deaths per thousand persons) to eleven or twelve. But it is impossible to accept the allocation of "credit" for the accomplishment which is so naively awarded to the medical or the public health worker in the discussions of the several diseases. Throughout the volume there are occasional remarks on the apparent changes which have occurred in the virulence of this or that disease; but these are largely forgotten in the analyses of the reasons for changes in disease incidence or in mortality. The pathologist, the bacteriologist and the epidemiologist are thoroughly familiar with cyclical recurrences of diseases — particularly in epidemic outbreaks. And they are generally agreed on only one score: the dynamics of the recurrences are still largely unknown. But the authors of the present volume are apparently unacquainted with the writings of Hirsch (though they quote him) and others of earlier years, of Newman, Newsholme, Brownlee, Young and others in England or of Chapin and a dozen others in the United States. Disputed interpretations on the causes for declines in the virulence of smallpox, scarlet fever, measles, influenza and other diseases do not receive any attention. The authors might profitably examine recent papers by Chapin and by Holst in the *Journal of Preventive Medicine*, and the last chapter in Jordan's recent monograph on Epidemic Influenza.

It is difficult to give specific criticisms without selection. A few citations may illustrate the type of material to which a reviewer must object. Is it generally accepted that "none who were truly vaccinated (against smallpox) contracted the disease . . . ."? (p. 320). The rapid decline of mortality from scarlet fever since 1880 (p. 348) is assigned to activities of health officers, though it is admitted (p. 353) that "For some reason which is not altogether clear, scarlet fever lost a good deal of its virulency during the second and third decades of the twentieth century" (p. 353)! and later (p. 401) appears this extraordinary summary and conclusion on scarlet fever: "Scarlet fever has become a disease of secondary importance. In spite of the increased density of population and the increased frequency and intimacy of contact of people, the disease has declined in prevalence. The theory is that the greatest decline in prevalence was that which occurred prior to 1897 and that the principal decline since then has been in the virulence of the disease — the case fatality rate. This is in a great measure true. For this latter improvement the better service of the medical profession and the elevation of the general standards of cleanliness have been the principal contributing factors. For the lessened prevalence of the disease, the health departments can claim most of the credit. Taking the field in its entirety the health agencies are entitled to somewhere near half of the credit." The decline of tuberculosis in mortality in Chicago since 1915 is accredited to the discovery of cases and the segregation of open cases not under the care of the family physician (p. 370). Have the authors forgotten to mention that a change in the state registration law permitted the deaths from tuberculosis among Chicago residents who die in Cook County outside the city limits to be omitted from the Chicago records? Have they overlooked the recent increase in tuberculosis mortality in Chicago? Was it Ross who discovered in 1897 that malaria is spread from one person to another only through the anopheles mosquito (p. 381)? For measles again, "For the six years ended with 1926 a still more favorable rate, an average of 4.4, prevailed. Better medical care of patients coupled with better public health service are the only two factors to which the improvement may reasonably be attributed" (p. 386). In the discussion of pneumonia (pp. 387-390) there is far too much righteous unction for the alleged recent decline in mortality. Not only pneumococcus typing, the use of serums and the practice of quarantine, but even prophylactic vaccination have been placed on a practical basis and their efficacies established! And on later pages there appears some balderdash about changes in the "span of life" and the meaning of death rates that no one familiar with the meaning of vital statistics would have written.

Apart from the objectionable items, of which a few examples have been noted, the reader will find food for thought in the story that is told in this volume. Early theories of disease, stories of epidemics of yellow fever, the separation of public health practice from medical supervision and licensure and other present-day obiter dicta give an historical flavor that warrants the volume.

GRUNDRISS DER PATHOLOGISCHEN ANATOMIE. VON PROF. DR. GOTTHOLD HERXHEIMER, Prosektor am städtischen Krankenhaus zu Wiesbaden. Spezieller Teil. Ed. 19 of Schmaus' Grundriss der Pathologischen Anatomie. Paper. Pp. 380, with 200, mostly colored, illustrations. Munich: J. F. Bergmann, 1927.

This volume on special pathology represents the remainder (pp. 315 to 695) of Herxheimer's textbook, and includes its index. The first part of the book, which deals with general pathology, was issued earlier in 1927 and has already been reviewed (ARCH. PATH. **3**:746, 1927). It is difficult to understand why this small textbook should have been issued in two volumes, especially since the reader of the second volume is constantly referred to pages included in the first.

The general plan of arrangement is that followed by the more pretentious German textbooks. The various sections of the volume are opened with preliminary

remarks on the structure and development of the organs to be discussed. Then follows the pathology, anatomy, ordered usually under the headings of congenital anomalies, circulatory disturbances, degenerations and allied conditions, inflammations, infectious granulations, tumors and parasites. The treatment of the different subjects in this part of the book seems more lucid than in the first part, probably because of the nature of the material, although in places it is compressed, almost like a quiz compend. This condensed style of presentation has enabled the author to incorporate in the small volume much of the newer knowledge on various topics. He also included in the twelve chapters making up this volume a thirteen page chapter on the general pathologic anatomy of the skin, which, although concise, is sufficiently complete for the student. Another chapter is devoted to acute infectious diseases, where, like in textbooks of internal medicine, each disease is discussed, from the pathologic standpoint, as a whole. In the section on the stomach, a pleasing feature is a good review of the effect of a long list of extraneous poisons on the organism, gathered under the heading of "poisonings."

However, compared with the special pathology of the seventeenth edition, this book shows no innovations. Of the numerous illustrations many seem to us poor, especially the photographs, and many of the drawings have gained nothing through coloration. Most of the enlargement of this edition is in the section dealing with the gastro-intestinal tract and the large abdominal glands. The chapter on the nervous system has always been a strong feature in this book since Schmaus. Perhaps the section on tuberculosis of the lung should be mentioned as being of exceptional excellence. In this Herxheimer departs from the purely descriptive methods and follows closely the well known Nicol-Aschoff classification of the lesions, whereby immunologic considerations are brought in relation with the anatomic changes. This book ought to be useful to Americans who wish to go abroad to study pathology, for besides other qualities, it is perhaps especially adapted for rapidly acquainting one with the continental approach to the subject.

PHYSIOLOGIE NORMALE ET PATHOLOGIQUE DU GLOBULIN (PLAQUETTE DE BIZZOZERO) [BLOOD PLATELETS]. By JACQUES ROSKAM. Price, 25 francs. Pp. 151 with illustrations. Paris: Presses Universitaires de France, 1927.

Only a decade ago Starling stated in his "Priciples of Human Physiology" that "the very existence of the blood platelets is still a matter of dispute." Today it is established beyond doubt that such an element exists in the blood. The discussion now is focused on the genesis of the platelets (plaquette de Bizzozero) and particularly on the rôle which they play in normal and pathologic conditions.

Although the subject is of relatively recent origin, an abundance of literature has been accumulated, judging from the references given by Roskam which number more than four hundred.

The problem has been of more interest to the clinician who has connected a number of hematopathologic conditions with the "third element" of the blood. The significance of the platelet is not limited only to the "bleeding and coagulation time." This element of the blood influences the circulation as a whole, and moreover it plays a rôle in the defensive mechanism of the organism and also in anaphylaxis. Chapter II in Roskam's book discusses, for instance, the rôle of the platelet in anaphylactic and anaphylactoid shocks, and the eleventh chapter is concerned with the significance of the platelets in humoral immunity.

In this monograph, Roskam discusses the multiple functions of the platelets. His work is both a résumé and a critical review of all that has been done on the subject up to date. "The time has come," says Roskam, "to gather different documents on this complicated question, to classify them, to eliminate the false from the truthful, and to separate sterile from fruitful hypotheses." In the discussion his rôle is, however, not that of a "reporter" only. He takes

an active part in the dispute, to which he is entitled by his personal diligent researches in this domain. He excuses himself before the reader for frequently speaking of his own experiments. He then adds: "J'ai l'humaine faiblesse de croire surtout ce que j'ai personnellement constaté."

The monograph, which is edited by the "Problemes Biologiques," contains nine chapters, each of which discusses one particular question concerning the rôle of the platelets in normal and pathologic physiology. The chapters are briefly summarized. The book is comprehensive, readable and interesting. It will serve as an excellent reference as well as a guide to those interested in this subject.

BEITRÄGE ZUR KENNTNIS DER MONGOLOIDEN MISSBILDUNG (MONGOLISMUS) AUF GRUND KLINISCHER, STATISTISCHER UND ANATOMISCHER UNTERSUCHUNGEN (DIE BEDEUTUNG DER GEBÄRMUTTERSCHLEIMHART UND DES AMNIONS FÜR DIE ATIOLOGIE UND PATHOGENESE DIESER MISSBILDUNG). VON W. M. VAN DER SCHEER, M.D. Price, 12 marks. Pp. 162, mit 44 abbildungen im text. Berlin: S. Karger, 1927.

As an inspector of the state supervision of the insane in Holland, van der Scheer had the opportunity of studying the records of 348 cases of mongolism, 150 of which were examined by him personally. About 5 per cent of the inmates of the Dutch psychopathic institutions are mongoloids.

Van der Scheer emphasizes that the similarity to the Mongolian race is merely a superficial one and that it is distinct only in early childhood, disappearing gradually with advancing age. Many of the abnormalities of the brain are nontypical and are commonly seen in severe cases of brachycephaly. There are differences in the measures between the skulls of mongoloid persons and representatives of the Mongolian race.

The author's observations fully agree with that of previous investigators in that the mongolian idiots usually are the last born children of large families and that the mothers at the time of their birth have reached an advanced age. He sees the essential factor of the mongolian deviations from the norm in an amniotic sac which is too narrow for the embryo, causing a compression of its head. This compression manifests itself in the sixth and seventh week of development. The disturbance of the development of the amnion, in turn, is due to a bad implantation of the ovum in an abnormal uterine mucosa. Hence, it is better to speak of a mongoloid malformation than of a mongolian idiocy.

Books Received

COMMITTEE OF THE PRIVY COUNCIL FOR MEDICAL RESEARCH. Report of the Medical Research Council for the Year 1926-1927. Price, 3 shillings net. Pp. 152. London: His Majesty's Stationery Office, 1928.

METHODEN DER HÄMOLYSEFORSCHUNG (MIT EINSCHLUSS DER HÄMAGGLUTINATION). Von Dr. Hans Sachs, Professor an der Universität, Direktor der wissenschaftl. Abteilung des Instituts für experimentelle Krebsforschung, Heidelberg, und Dr. Alfred Klopstock, Privatdozent an der Universität, Assistent der wissenschaftl. Abteilung des Instituts für experimentelle Krebsforschung, Heidelberg. Price, 13 marks. Pp. 232. Berlin: Urban & Schwarzenberg, 1928.

CLINICAL PHYSIOLOGY (A SYMPTOM ANALYSIS) IN RELATION TO MODERN DIAGNOSIS AND TREATMENT. A Text for Practitioners and Senior Students of Medicine. By Robert John Stewart McDowall, D.Sc., M.B., F.R.C.P. (Edinburgh), Professor of Physiology, King's College, University of London. With an Introduction by W. P. Halliburton, LL.D., F.R.C.P., F.R.S., Emeritus Professor of Physiology, King's College, University of London. Pp. 383. New York: D. Appleton & Co., 1927.

DIE AETIOLOGIE DER BÖSARTIGEN GESCHWÜLSTE. Nach dem gegenwartigen Stande der klinischen Erfahrung und der experimentellen Forschung. Von Professor Dr. Carl Lewin, Berlin. Price, 18 marks. Pp. 231. Berlin: Julius Springer, 1928.

DIE GEWEBEZÜCHTUNG IN VITRO. Von V. Bisceglie und A. Juhász-Schaffer am Institut für Allgemeine Pathologie der Universität zu Modena. Price, 24 marks. Pp. 355, mit 71 abbildungen. Berlin: Julius Springer, 1928.

POST MORTEMS AND MORBID ANATOMY. By Theodore Shennan, M.D., F.R.C.S. (Edinburgh), Professor of Pathology in the University of Aberdeen. Second Edition. Price, 25 shillings. Pp. 664, illustrated. London: Faber & Gwyer, Ltd., 1927.

ALUMINUM COMPOUNDS IN FOOD. Including a Digest of the Report of the Referee Board of Scientific Experts on the Influence of Aluminum Compounds on the Nutrition and Health of Man. By Ernest Ellsworth Smith, Ph.D., M.D., Fellow and Former President, New York Academy of Sciences, Fellow of the New York Academy of Medicine, etc. Price, $7. Pp. 378. New York: Paul B. Hoeber, Inc., 1928.

ORGANIC INHERITANCE IN MAN. By F. A. E. Crew, M.D., D.Sc., Ph.D., Director of the Animal Breeding Research Department, The University, Edinburgh. Price, 12/6 net. Pp. 214. London: Oliver and Boyd, 1927.

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